Li, B.
09/720513

(FILE 'CAPLUS' ENTERED AT 09:22:54 ON 26 FEB 2002)
L1 114697 SEA FILE=CAPLUS ABB=ON PLU=ON IGA OR IGG OR IGM OR (IG OR IMMUNOGLOBULIN OR IMMUNO GLOBULIN)(1W)(A OR G OR M) OR B(W)(CELL OR LYMPHOCYT?)
L2 33579 SEA FILE=CAPLUS ABB=ON PLU=ON L1(S)ANTIBOD?
L3 121 SEA FILE=CAPLUS ABB=ON PLU=ON L2 AND (MUCOUS OR MUCOSAL OR MUCUS)(5A)MEMBRAN?
L4 21 SEA FILE=CAPLUS ABB=ON PLU=ON L3 AND ADMIN?

L4 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:208077 CAPLUS
DOCUMENT NUMBER: 134:242662
TITLE: Pharmaceutical composition to be **administered** through **mucous membrane**
INVENTOR(S): Gaubert, Sophie; Laversanne, Rene
PATENT ASSIGNEE(S): Capsulis, Fr.
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001019335	A2	20010322	WO 2000-FR2523	20000913
WO 2001019335	A3	20011004		
W: AU, CA, JP, MX, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2798288	A1	20010316	FR 1999-11465	19990914
FR 2798288	B1	20011130		

PRIORITY APPLN. INFO.: FR 1999-11465 A 19990914

AB The invention concerns a novel use of onion-structured multilamellar vesicles having a liq.-crystal internal structure formed by stacked concentric double layers based on amphiphilic agents with layers of water, aq. soln. or soln. of polar liq. and wherein is incorporated at least an antigen for making a compn., in particular a pharmaceutical compn., and more particularly a vaccine compn., to be **administered** through a **mucous membrane** to induce a **mucous** and/or serumal systemic response and/or for protecting the system against infection caused by said antigen. The invention also concerns a vaccine method through a **mucous membrane** and a method for producing **antibodies**, in particular, **IgA**. The invention is particularly applicable for intranasal **administration**. Pharmaceutical vesicles contg. potassium oleate 0.50, ethoxylated lauryl alc. 0.20, lanolin cholesterol 0.50, cholesterol-3-sulfate 0.20, PBS 20.0, soya lecithin 45.5, and human serum albumin 20.0% were prepd. The vesicles were **administered** nasally to guinea pigs and HSA-specific IgA and IgG were measured.

L4 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:101291 CAPLUS
DOCUMENT NUMBER: 134:161880
TITLE: cDNAs encoding the Flt-3 receptor ligand and there use as adjuvants in vector vaccines

INVENTOR(S): Hermanson, Gary George
PATENT ASSIGNEE(S): Vical Inc., USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001009303	A2	20010208	WO 2000-US20679	20000731
WO 2001009303	A3	20010816		

W: CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1999-146170 P 19990730

AB A method of increasing the strength of the immune response of vector vaccines using an expression vector for the Flt3 ligand is described. The vaccines are made of independent non-integrating expression vectors: one encodes the antigen or a cytokine and the other encodes the Flt3 ligand. The present invention also provides a method broadly directed to improving immune response of a vertebrate in need of immunotherapy by **administering** in vivo, into a tissue of a vertebrate, a Flt-3 ligand-encoding polynucleotide and one or more antigen- or cytokine-encoding polynucleotides. The polynucleotides are incorporated into the cells of the vertebrate in vivo, and a prophylactically or therapeutically effective amt. of a Flt-3 ligand and one or more antigens is produced in vivo.

L4 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:688114 CAPLUS
DOCUMENT NUMBER: 133:271614
TITLE: Vaccine composition comprising penetration enhancers
INVENTOR(S): Alpar, Hazire Oya; Somavarapu, Satyanarayana; Williamson, Ethel Diane; Baillie, Leslie William James
PATENT ASSIGNEE(S): The Secretary of State for Defence, UK
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000056361	A2	20000928	WO 2000-GB1104	20000323
WO 2000056361	A3	20010301		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1163001 A2 20011219 EP 2000-912777 20000323
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: GB 1999-6694 A 19990324
GB 1999-6696 A 19990324
WO 2000-GB1104 W 20000323

AB A pharmaceutical compn. comprising: (i) a biol. active agent; (ii) an adjuvant chem. which increases the effect of the biol. active agent, said chem. selected from one or more of: (A) a polyamino acid, (B) a vitamin or vitamin deriv., (C) cationic pluronics, (D) a clathrate, (E) a complexing agent, (F) cetrimides, (G) an S-layer protein, or (H) methyl-glucamine; (iii) a pharmaceutically acceptable carrier or diluent, provided that when the chem. (ii) above is selected from (D) or (E), the biol. active agent is an agent which is capable of generating a protective immune response in an animal to which it is **administered**. The compn., which may be in the form of a soln. or particles such as microspheres or liposomes, is particularly useful for mucosal **administration** of vaccines esp. be the intra-nasal route or by parenteral routes. Mice were intranasally immunized with admixed F1 (5.mu.g) and V (1.mu.g) antigens of Yersinia pestis in conjunction with 2.5% cyclodextrin (I). Serum was analyzed on the day 14 for the presence of anti-V and anti-F1 **IgG antibodies**. I had significant absorption enhancer effects as compared to the controls.

L4 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:358971 CAPLUS
DOCUMENT NUMBER: 133:103523
TITLE: Effect of preexisting immunity to Salmonella on the immune response to recombinant Salmonella enterica serovar typhimurium expressing a Porphyromonas gingivalis hemagglutinin
AUTHOR(S): Kohler, James J.; Pathangey, Latha B.; Gillespie, Sheila R.; Brown, Thomas A.
CORPORATE SOURCE: Department of Oral Biology, University of Florida, Gainesville, FL, 32610, USA
SOURCE: Infect. Immun. (2000), 68(6), 3116-3120
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recombinant Salmonella strains expressing foreign heterologous genes have been extensively studied as live oral vaccine delivery vectors. We have investigated the mucosal and systemic immune responses following oral immunization with a recombinant Salmonella enterica serovar Typhimurium expressing the hemagglutinin HagB from Porphyromonas gingivalis, a suspected etiol. agent of adult periodontal disease. We have previously shown a primary mucosal and systemic response following oral immunization with .chi.4072/pDMD1 and recall responses following boosting at 14 wk after primary immunization. In this study, we examd. the effects of earlier boosting as well as the effects of deliberately induced immunity to the Salmonella carrier strain on subsequent immune responses. Mice boosted at week 7 following immunization, a point which corresponded to the peak of the primary response, generally showed lower responses than those boosted at week 14. When mice were

preimmunized with the Salmonella carrier alone and then immunized with the recombinant strain 7 or 14 wk later, significant redns. were seen for serum **IgG antibodies** at week 14 and for salivary **IgA** at week 7. No redns. were seen in serum **IgA** or vaginal wash **IgA antibodies** . Mice appear to be refractory to boosting with orally **administered** salmonellae at 7 wk. Deliberate immunization with the carrier strain did not appreciably affect recall responses at 14 wk, with the exception of the serum IgG responses, nor did it affect colonization of the Peyer's patches.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:15035 CAPLUS
DOCUMENT NUMBER: 132:69299
TITLE: Mucosal targeting immunization comprising immunogens
INVENTOR(S): Jourdier, Therese; Moste, Catherine; Meignier, Bernard
PATENT ASSIGNEE(S): Pasteur Merieux Serums & Vaccins, Fr.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000218	A1	20000106	WO 1999-FR1554	19990628
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9943761	A1	20000117	AU 1999-43761	19990628
EP 1087788	A1	20010404	EP 1999-926558	19990628
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
US 2001021384	A1	20010913	US 2000-746581	20001221

PRIORITY APPLN. INFO.: FR 1998-8354 A 19980626
WO 1999-FR1554 W 19990628

AB The invention concerns the use of an immunogen specific of a pathogenic agent with a gateway in the buccal **mucous membrane** region, for producing a vaccine compn. to be **administered** in the floor of the mouth in a human being so as to develop directly a local response in **IgA antibodies** and in **B cells** secreting **IgA** in the buccal **mucous membrane**, saliva and ganglions draining said **mucous membrane** . The invention also concerns a vaccine compn. capable of being applied in the floor of the mouth in a human being to induce local

and systemic immunity in **IgA antibodies**, substantially consisting of a material adhering or not to the buccal **mucous membrane** and contg. an immunogen specific of the pathogenic agent with a gateway into the buccal **mucous membrane**. Capsules contg. starch and hydroxyapatite particles comprising lyophilized antigens of cytomegalovirus or hepatitis A were prepd. The capsules were slowly dissolved inside the mouth. The hydroxyapatite facilitated the penetration of the immunogens through the mucosa.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:15033 CAPLUS
DOCUMENT NUMBER: 132:69298
TITLE: Mucosal targeting immunization comprising immunogens
INVENTOR(S): Jourdier, Therese; Moste, Catherine; Meignier, Bernard
PATENT ASSIGNEE(S): Pasteur Merieux Serums & Vaccins, Fr.
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000217	A1	20000106	WO 1999-FR1539	19990625
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9943754	A1	20000117	AU 1999-43754	19990625
EP 1089758	A1	20010411	EP 1999-926545	19990625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				

PRIORITY APPLN. INFO.: FR 1998-8353 A 19980626
WO 1999-FR1539 W 19990625

AB The invention concerns the use of an immunogen specific of a pathogenic agent having a gateway in a **mucous membrane** for producing an immunogenic compn. to be **administered** to a human by parenteral route at the surface of part of the body distinct from the **mucous membrane** so as to directly develop a local response in **IgA**, **IgG** and/or **IgM antibody** in said **mucous membrane**. Vaccines against Herpes simplex, Candida, Chlamydia, human Papilloma virus, genital Mycoplasma, and Treponema pallidum was prepd. and injected to the buttocks muscle to stimulate local **IgA antibody** response in rectal, genital and urinary mucosa.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:287072 CAPLUS
DOCUMENT NUMBER: 131:86630
TITLE: A novel and effective intranasal immunization strategy for respiratory syncytial virus
AUTHOR(S): Tebbey, Paul W.; Unczur, Catherine A.; LaPierre, Natisha A.; Hancock, Gerald E.
CORPORATE SOURCE: Dep. Immunol. Res., Wyeth-Lederle Vaccines Pediatrics, West Henriette, NY, USA
SOURCE: Viral Immunol. (1999), 12(1), 41-45
CODEN: VIIMET; ISSN: 0882-8245
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In designing subunit vaccination strategies for respiratory syncytial virus (RSV), immunization by mucosal routes may present a realistic alternative to parenteral **administration** for inducing protective immune responses. To this end, we have utilized the BALB/c mouse model and an adjuvant formulation contg. caprylic/capric glycerides (CCG) and polyoxyethylene-20-sorbitan monolaurate (PS). The intranasal (i.n.) delivery of purified natural F protein (3 .mu.g per vaccine) formulated with CCG-PS resulted in the generation of statistically heightened serum anti-F protein **IgG**, IgG1, IgG2b, and **IgA antibodies**. In addn., the presence of locally produced anti-F protein IgA was demonstrated in both vaginal and nasal washes of vaccinated mice. That prodn. of specific serum and mucosal Igs resulted in functional immune responses was shown in neutralizing antibody assays and protection of mouse lungs against subsequent live virus challenge. Consequently, we propose a novel vaccine formulation composed of purified natural RSV F protein in CCG-PS as a viable intranasal immunogen to stimulate anti-RSV immune responses in humans.
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:194278 CAPLUS
DOCUMENT NUMBER: 130:236477
TITLE: Enhancement of mucosal antibody responses by interleukin-6
INVENTOR(S): Derman, Eva
PATENT ASSIGNEE(S): The Public Health Research Institute of the City of New York, Inc., USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9913092 A1 19990318 WO 1998-US19183 19980911
W: AU, CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
AU 9894847 A1 19990329 AU 1998-94847 19980911
PRIORITY APPLN. INFO.: US 1997-58528 P 19970911
WO 1998-US19183 W 19980911

AB The invention provides a transgenic mouse overexpressing human interleukin-6 and methods of enhancing mucosal IgA responses in which interleukin-6 is delivered to the mucosal immune system. The transgenic mouse provides mucosal-specific expression of interleukin-6 within the submandibular gland. This is achieved by construction of a fusion gene contg. the coding sequence for human IL-6 linked to the 5' regulatory region of the mouse major urinary protein 5 gene. In addn., enhancement of the mucosal IgA response is achieved either by oral **administration** of the cytokine or by genetic immunization.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:64958 CAPLUS
DOCUMENT NUMBER: 130:138289
TITLE: Pseudomonas exotoxin A-like chimeric immunogens for eliciting a secretory IgA-mediated immune response
INVENTOR(S): Fitzgerald, David J.; Mrsny, Randall J.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA; Genentech, Inc.
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9902712	A1	19990121	WO 1998-US14336	19980710
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9883929	A1	19990208	AU 1998-83929	19980710
EP 1000162	A1	20000517	EP 1998-934405	19980710
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-56924 P 19970711
WO 1998-US14336 W 19980710

AB This invention provides methods of eliciting a secretory IgA-mediated immune response in a subject by **administering** a Pseudomonas exotoxin (PE) A-like chimeric immunogens that include

a non-native epitope in the Ib domain of Pseudomonas exotoxin. The chimeric immunogen comprises (1) a cell recognition domain that binds to cell surface receptor on mucosal surface, (2) a translocation domain (PE domain II) to effect translocation to cell cytosol, (3) a foreign epitope domain, and (4) an endoplasmic reticulum retention domain. The foreign epitope domain is derived from epitope of HIV-1, herpes virus, vaccinia, cytomegalovirus, yersinia or vibrio. Compns. comprising secretory **IgA antibodies** that specifically recognize an epitope of HIV-1 also are provided.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:621321 CAPLUS
DOCUMENT NUMBER: 129:235638
TITLE: Construction of cationic lipid complex-polynucleotides-contg.liposomes for gene delivery to mucosal epithelium for immunization or therapeutic purposes
INVENTOR(S): Davis, Heather Lynn; Jessee, Joel; Gebeyehu, Gulilat
PATENT ASSIGNEE(S): Can.
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9840499	A1	19980917	WO 1997-US3421	19970310
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9719871	A1	19980929	AU 1997-19871	19970310

PRIORITY APPLN. INFO.: WO 1997-US3421 19970310

AB Disclosed are compns. and method for transfecting mammalian mucosal epithelia with nucleic acid/cationic lipid complexes. The nucleic acid/cationic lipid complexes may be **administered**, for example, intranasally or directly into the lungs. The best results are obtained when the lipid mixed with the max. amt. of DNA that it can complex. Thus, cationic lipids are complexed with a polynucleotides coding for immunogenic antigens in mice. Hybridomas are constructed by fusing **B-lymphocytes** with myeloma cells, and pos. clones are selected which produce anti-immunogen **antibody**. Suitable cationic lipids include DOTMA, DOTAP, and DORI-esters. Neutral lipids that can be used include lecithins, phosphotidylethanolamine, phosphatidylethanolamines (e.g. DOPE, OPPE), and distearoylphosphatidylethanolamine. Cationic sterol derivs., such

as DC-Chol can also be used. Polyclonal and monoclonal antibodies and antisense oligonucleotides are also claimed effective to gene therapy. The method is tested in a mouse system.

L4 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:616820 CAPLUS
DOCUMENT NUMBER: 130:36989
TITLE: Mapping of B epitopes in GRA4, a dense granule antigen of Toxoplasma gondii and protection studies using recombinant proteins **administered** by the oral route
AUTHOR(S): Mevelec, Marie-Noelle; Mercereau-Puijalon, Odile; Buzoni-Gatel, Dominique; Bourguin, Isabelle; Chardes, Thierry; Dubremetz, Jean-Francois; Bout, Daniel
CORPORATE SOURCE: CJF INSERM 93-09, Immunologie des Maladies Infectieuses, Equipe associee INRA d'Immunologie Parasitaire, UFR des Sciences Pharmaceutiques, Tours, 37200, Fr.
SOURCE: Parasite Immunol. (1998), 20(4), 183-195
CODEN: PAIMD8; ISSN: 0141-9838
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB GRA4, a dense granule protein of Toxoplasma gondii elicits both mucosal and systemic immune responses following oral infection of mice with cysts. We studied the antigenicity and immunogenicity of truncated and sol. forms of GRA4 expressed as glutathione S-transferase fusion proteins in Escherichia coli. Protein C (amino-acids 297-345) was particularly well recognized by serum **IgG antibodies**, milk **IgA antibodies** and intestinal IgA **antibodies** from T. gondii infected mice and by serum **IgG antibodies** from T. gondii infected humans and T. gondii infected sheep. One major B epitope was localized within the last 11 C-terminal residues of GRA4. A second epitope, recognized with lower frequency, was mapped within the region 318-334. In contrast, the N domain of GRA4 (amino acids 25-276) was poorly recognized. Oral immunization of C57BL/6 mice with N, C or NC (amino acids 25-276 fused to 297-345) in assocn. with cholera toxin induced a significant prodn. of serum anti-GRA4 **IgG antibodies** but a weak and inconsistent intestinal anti-GRA4 **IgG antibody** response and afforded partial resistance to oral infection with T. gondii. These results provide new mol. and immunol. understanding of GRA4 and indicate that it is a potential candidate for oral vaccination against T. gondii.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:244025 CAPLUS
DOCUMENT NUMBER: 129:26743
TITLE: Intranasal immunization of mice with herpes simplex virus type 2 recombinant gD2: the effect of adjuvants on mucosal and serum antibody responses
AUTHOR(S): Ugozzoli, M.; O'Hagan, D. T.; Ott, G. S.

CORPORATE SOURCE: Chiron Vaccines, Emeryville, CA, USA
SOURCE: Immunology (1998), 93(4), 563-571
CODEN: IMMUAM; ISSN: 0019-2805
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mucosal immunization offers the potential for inducing **IgA antibody** responses in the vagina, the site of infection for many viruses, including herpes simplex type 2 (HSV-2). To investigate this possibility, mice were immunized intranasally with 10 .mu.g glycoprotein D2 (gD2) from HSV combined with a series of adjuvants of proven efficacy; the oil in water emulsion MF59, poly(D,L-lactide-co-glycolide) microparticles (PLG) (encapsulated or co-**administered**), immune-stimulating complexes (iscoms) (incorporated or co-**administered** with iscomatrix) and the genetically detoxified enterotoxin from Escherichia coli, LT-K63. Encapsulation of gD2 into PLG microparticles, incorporation of gD2 into iscoms and co-**administration** of gD2 with LT-K63 induced mucosal **IgA antibody** responses (nasal wash, saliva and vaginal wash) which were greater than those induced by i.m. **administration** of gD2 with MF59. Intranasal immunization with these formulations also induced substantial levels of serum **IgG** and neutralizing **antibodies**. These studies demonstrated that intranasal immunization with potent adjuvants is an effective means to induce mucosal antibody responses, even in the lower genital tract.

L4 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:214106 CAPLUS
DOCUMENT NUMBER: 128:320287
TITLE: Intranasal **administration** of a meningococcal outer **membrane** vesicle vaccine induces persistent local **mucosal** antibodies and serum antibodies with strong bactericidal activity in humans
AUTHOR(S): Haneberg, Bjorn; Dalseg, Rolf; Wedege, Elisabeth; Hoiby, E. Arne; Haugen, Inger Lise; Oftung, Fredrik; Andersen, Svein Rune; Naess, Lisbeth Meyer; Aase, Audun; Michaelsen, Terje E.; Holst, Johan
CORPORATE SOURCE: Department of Vaccinology, National Institute of Public Health, Oslo, N-0403, Norway
SOURCE: Infect. Immun. (1998), 66(4), 1334-1341
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A nasal vaccine, consisting of outer membrane vesicles (OMVs) from group B Neisseria meningitidis, was given to 12 volunteers in the form of nose drops or nasal spray 4 times at weekly intervals, with a fifth dose 5 mo later. Each nasal dose consisted of 250 .mu.g of protein, equiv. to 10 times the i.m. dose that was **administered** twice with a 6-wk interval to 11 other volunteers. All individuals given the nasal vaccine developed **IgA antibody** responses to OMVs in nasal secretions, and 8 developed salivary **IgA antibodies** which persisted for at least 5 mo. I.m. immunizations did not lead to antibody responses in the secretions.

Modest increases in serum IgG **antibodies** were obtained in 5 volunteers who had been immunized intranasally, while 10 individuals responded strongly to the i.m. vaccine. Both the serum and secretory antibody responses reached a max. after 2-3 doses of the nasal vaccine, with no booster effect of the fifth dose. The pattern of serum antibody specificities against the different OMV components after intranasal immunizations was largely similar to that obtained with the i.m. vaccine. Five and 8 vaccinees in the nasal group developed persistent increases in serum bactericidal titers to the homologous meningococcal vaccine strain expressing low and high levels, resp., of the outer membrane protein Opc. Thus, meningococcal OMVs possess the structures necessary to initiate systemic as well as local mucosal immune responses when presented as a nasal vaccine. Although the serum antibody levels were less conspicuous than those after i.m. vaccinations, the demonstration of substantial bactericidal activity indicates that a nonproliferating nasal vaccine might induce antibodies of high functional quality.

L4 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:333469 CAPLUS
DOCUMENT NUMBER: 126:313472
TITLE: A nontoxic mutant of cholera toxin elicits Th2-type responses for enhanced mucosal immunity
AUTHOR(S): Yamamoto, Shingo; Kiyono, Hiroshi; Yamamoto, Masafumi; Imaoka, Koichi; Yamamoto, Miho; Fujihashi, Kohtaro; Van Ginkel, Frederik W.; Noda, Masatoshi; Takeda, Yoshifumi; McGhee, Jerry R.
CORPORATE SOURCE: Dep. Micribool. Oral Biol., Immunobiol. Vaccine Cent., Univ. Alabama, Med. Cent., Birmingham, AL, 35294-2170, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1997), 94(10), 5267-5272
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have characterized a nontoxic mutant of cholera toxin (CT) as a mucosal adjuvant in mice. The mutant CT was made by substitution of serine with phenylalanine at position 61 of the A subunit (S61F), which resulted in the loss of ADP ribosyltransferase activity and toxicity. Mice were intranasally immunized with ovalbumin, tetanus toxoid, or influenza virus either alone or together with mutant CT S61F, native CT, or recombinant CT-B. Mice immunized with these proteins plus S61F showed high serum titers of protein-specific **IgG** and **IgA antibodies** that were comparable to those induced by native CT. Further, high protein-specific **IgA antibody** responses were obsd. in nasal and vaginal washes, saliva, and fecal exts. as well as increased nos. of **IgG** and **IgA antibody**-forming cells in cervical lymph nodes and lung tissues of mice intranasally immunized with these proteins and S61F or native CT, but not with recombinant CT-B or protein alone. Both S61F and native CT enhanced the induction of ovalbumin-specific CD4+ T cells in lung and splenic tissues, and these T cells produced a Th2-type cytokine pattern of interleukin 4 (IL-4), IL-5, IL-6, and IL-10 as detd. by anal. of secreted proteins and by quantitation of

cytokine-specific mRNA. These results have shown that mutant CT S61F is an effective mucosal adjuvant when **administrated** intranasally and induces mucosal and systemic antibody responses which are mediated by CD4+ Th2-type cells.

L4 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:184693 CAPLUS
DOCUMENT NUMBER: 126:170403
TITLE: Viral suppression, treatment and prevention of viral infections
INVENTOR(S): Davis, Gary R.
PATENT ASSIGNEE(S): Gkc Research, Inc., USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9702839	A1	19970130	WO 1996-US11612	19960712
W: CA, CN, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

PRIORITY APPLN. INFO.: US 1995-1115 19950713
US 1995-551676 19951101

AB It has been discovered that it is possible to **administer** neutralizing antibodies produced by a first mammal into a second mammal for the purpose of treating or preventing viral infections, with the first and second mammals being of either the same or different species. The neutralizing antibodies are mixed with the virus of interest such that the neutralizing antibodies bind at least one but not all epitopes of the virus so as to render the virus noninfectious while maintaining immunogenicity. The neutralizing antibodies may be **administered** as a serum transfusion, a vaccine, or a topical prepn. on condoms or latex rubber gloves. The antibodies may also useful for neutralizing caprine encephalitis virus in livestock. Goat neutralizing antibodies against Simian immunodeficiency virus were prepd. and used to attenuate SIV, HIV or other virus to produce vaccine.

L4 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:147342 CAPLUS
DOCUMENT NUMBER: 126:216564
TITLE: Size effect on systemic and mucosal immune responses induced by oral **administration** of biodegradable microspheres
AUTHOR(S): Tabata, Yasuhiko; Inoue, Yoshiharu; Ikada, Yoshito
CORPORATE SOURCE: Research Center for Biomedical Engineering, Kyoto University, Kyoto, 606, Japan
SOURCE: Vaccine (1996), 14(17/18), 1677-1685
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Induction of systemic and mucosal immune responses following oral

administration of biodegradable poly(DL-lactic acid) (PDLLA) microspheres contg. a model antigen, ovalbumin (OVA) was studied using microspheres with different av. diams. of 0.6, 1.0, 4.0, 7.0, 11.0, 15.0, 21.0, and 26.0 .mu.m. They were prepd. from a double emulsion with the solvent evapn. method, followed by size fractionation on counterflow elutriation. OVA was released from the microspheres in vitro over 80 days, irresp. of their size. Prodn. of the serum anti-OVA **IgG antibody** and secretory OVA-specific **IgA antibody** in the mice gut was assessed following the oral **administration** of PDLLA microspheres contg. OVA. Microspheres with a diam. of 4.0 .mu.m enhanced the serum **antibody** in contrast with that of free OVA, but were not effective in inducing the gut secretion of **IgA antibody**. On the other hand, OVA-contg. microspheres with a diam. of 7.0 .mu.m enhanced IgA secretion to a significant extent compared with free OVA, whereas those with 26.0 .mu.m in diam. were ineffective. Body distribution study revealed that the amt. of microspheres taken up into Peyer's patches (PP) increased with the increasing size up to 11.0 .mu.m, thereafter decreased, and finally became zero when their diams. were 21.0 .mu.m or larger. The microspheres taken up into PP were translocated to the spleen, but no microspheres were noticed in the spleen when the size was larger than 5 .mu.m. After being taken up into PP, microspheres <5 .mu.m in diam. seemed to be transported to the spleen, a systemic lymphoid tissue, where the released antigen stimulated a serum **antibody** response, but larger microspheres probably remained at PP without being translocated to the spleen over the course of their antigen release, leading to induction of **IgA** secretion. The body distribution pattern of microspheres following the PP uptake was a key factor to regulate the induction of systemic and mucosal immune responses.

L4 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:423743 CAPLUS
DOCUMENT NUMBER: 125:123386
TITLE: Preparation and characterization of a biodegradable microparticle antigen/cytokine delivery system
AUTHOR(S): Rafferty, D. E.; Elfaki, M. G.; Montgomery, P. C.
CORPORATE SOURCE: School Medicine, Wayne State University, Detroit, MI, 48201, USA
SOURCE: Vaccine (1996), 14(6), 532-538
CODEN: VACCDE; ISSN: 0264-410X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Biodegradable microparticles (MPs) were prepd. to contain dinitrophenylated bovine serum albumin (DNP-BSA) and the cytokines [illegible]kin (IL)-5 and IL-6. The conformational integrity of these [illegible] by SEM. DNP-BSA was evaluated, postentrapment, by a [illegible]ssay, SDS-PAGE, isoelec. focusing, Western [illegible] spectrophotometric anal. The bioactivity of the [illegible] was measured using bioassays. Ocular-topical [illegible] **administration** of loaded MPs induced [illegible]A and vaginal wash (VW) IgA responses which [illegible] days post secondary immunization (P2.degree.). [illegible] elicited serum IgG and tear IgA responses up to [illegible]tiary immunization (P3.degree.). VW IgA responses

persisted up to 45 days and 140 days P3.degree. following OT and IP delivery, resp. Overall, the inclusion of cytokines in antigen contg. MPs enhanced tear **IgA antibody** levels following OT delivery P2.degree., while elevated VW **IgA** responses occurred following IP delivery P2.degree. and P3.degree.. These data demonstrate that antigen/cytokine loaded MPs can potentiate long-term mucosal antibody responses at both target and distal effector sites as well as elicit circulating antibodies.

L4 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:416581 CAPLUS
DOCUMENT NUMBER: 122:184955
TITLE: Protection of mice against an influenza virus infection by oral vaccination with viral nucleoprotein incorporated into immunostimulating complexes
AUTHOR(S): Scheepers, K.; Becht, H.
CORPORATE SOURCE: Institut fur Virologie, Justus-Liebig-Universitat Giessen, Giessen, D-35392, Germany
SOURCE: Med. Microbiol. Immunol. (1994), 183(5), 265-73
CODEN: MMIYAO; ISSN: 0300-8584
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Influenza A virus nucleoprotein (NP) was integrated into immunostimulating complexes (ISCOMs) after attachment of bacterial lipopolysaccharide to the antigen. Oral immunization with these NP-ISCOMs protected mice fully against an otherwise lethal challenge infection with an unrelated influenza virus subtype without the appearance of severe clin. signs or extensive pathol. lesions in the lungs. Mice immunized with analogous bovine serum albumin-incorporated ISCOMs all died. After oral immunization, high titers of NP-specific **antibodies**, particularly **IgA** , could be detected in the bronchoalveolar fluid and in the blood serum. No cytotoxic lymphocytes were demonstrated in the spleens or the lungs of vaccinated mice, and no anti-NP antibody-dependent cytolysis of infected host cells was mediated by complement or in the form of an antibody-dependent cell cytotoxicity. However, a vigorous delayed-type hypersensitivity reaction was produced after probing vaccinated animals with purified NP. No comparable protective immunity or antibody response was induced by a strictly intragastric **administration** of NP-ISCOMs. Thus, the general and local immune response in the lungs was primarily stimulated through contact of NP-ISCOMs with the **mucous membrane** of the oro-pharyngeal cavity and cytotoxic effects did not play a major role for the establishment of the protective immunity. Partial protection against a lethal challenge was obsd. in chickens immunized with NP-ISCOMs in the drinking water.

L4 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:158892 CAPLUS
DOCUMENT NUMBER: 116:158892
TITLE: Synthetic poly-Ig receptor, receptor-antibody complexes, production and use thereof
INVENTOR(S): Kraehenbuhl, Jean Pierre; Weltzin, Richard A.; Neutra, Marian R.
PATENT ASSIGNEE(S): Harvard College, USA; Institut Suisse de Recherches Experimentales sur le Cancer
SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9116061	A1	19911031	WO 1991-US2604	19910416
W: AU, BG, BR, CA, FI, HU, JP, KP, KR, NO, RO, SU				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
CN 1057785	A	19920115	CN 1991-103351	19910415
CA 2059289	AA	19911017	CA 1991-2059289	19910416
AU 9177926	A1	19911111	AU 1991-77926	19910416
ZA 9102837	A	19920325	ZA 1991-2837	19910416
EP 480014	A1	19920415	EP 1991-909070	19910416
EP 480014	B1	19961113		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
BR 9105717	A	19920721	BR 1991-5717	19910416
JP 05501118	T2	19930304	JP 1991-508821	19910416
HU 63059	A2	19930728	HU 1992-136	19910416
RO 109703	B1	19950530	RO 1991-148980	19910416
AT 145137	E	19961115	AT 1991-909070	19910416
ES 2097207	T3	19970401	ES 1991-909070	19910416
RU 2124050	C1	19981227	RU 1991-5010958	19910416
NO 9104946	A	19920212	NO 1991-4946	19911213
AU 9477715	A1	19950406	AU 1994-77715	19941103
AU 687443	B2	19980226		

PRIORITY APPLN. INFO.: US 1990-510161 A 19900416
WO 1991-US2604 A 19910416

AB Poly-Ig **antibodies** (particularly monoclonal **IgAs**) are complexed with a stabilizer protein derived from the poly-Ig receptor (particularly a recombinant receptor-derived stabilizer protein), which includes a .gtoreq.1 poly-Ig binding domain of the receptor, and substantially lacks any C-terminal transmembrane or intracellular poly-Ig receptor domains. The stabilized complex can be used as a passive vaccine **administration** to mucosal surfaces. Methods for in vivo screening of monoclonal poly-Ig are also disclosed. Methods of generating the complex using a monolayer of anchorage-dependent epithelial cells engineered to make poly-Ig receptor are also disclosed. Hybridomas for manuf. of monoclonal IgA are made by harvesting lymphoid cells from mucosal tissue (e.g. Peyer's patches) rich in such cells.

L4 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:130062 CAPLUS
DOCUMENT NUMBER: 102:130062
TITLE: **IgA antibodies** to oral and ocular bacteria in human external secretions
AUTHOR(S): Gregory, R. L.; Schoeller, M.; Filler, S. J.; Crago, S. S.; Prince, S. J.; Allansmith, M. R.; Michalek, S. M.; Mestecky, J.; McGhee, J. R.
CORPORATE SOURCE: Dep. Microbiol., Univ. Alabama, Birmingham, AL, 35294, USA
SOURCE: Protides Biol. Fluids (1985), Volume Date 1984, 32, 53-6
CODEN: PBFPA6; ISSN: 0079-7065

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human saliva contains secretory **IgA** (sIgA) **antibodies** to Streptococcus mutans; however, lower **antibody** levels to serotype c than other serotypes of S. mutans are found. Oral challenge with S. mutans c and d resulted in implantation of c but not d, suggesting that naturally occurring salivary **IgA antibodies** regulate S. mutans colonization. Saliva, tears, and milk contain naturally occurring sIgA antibodies to S. mutans and ocular bacteria, implying that these bacteria stimulate gut-assocd. lymphoreticular tissue (GALT) leading to sIgA responses in distant mucosal sites. Oral **administration** of S. mutans c to humans induced elevated levels of sIgA antibodies in external secretions and lowered no. of S. mutans in dental plaque. Peripheral blood lymphocyte cultures stimulated with pokeweed mitogen and S. mutans gave antigen-specific IgA responses. These results show that ingested bacterial antigens stimulate GALT, and that precursor-IgA B cells from this tissue migrate via the circulation to distant mucosal tissues, supporting the concept of a common mucosal IgA immune system in humans.

L4 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:129934 CAPLUS
DOCUMENT NUMBER: 102:129934
TITLE: Evidence for a common mucosal immune system in humans
AUTHOR(S): Mestecky, J.; McGhee, J. R.; Russell, M. W.; Michalek, S. M.; Kutteh, W. H.; Gregory, R. L.; Scholler-Guinard, M.; Brown, T. A.; Crago, S. S.
CORPORATE SOURCE: Univ. Alabama, Birmingham, AL, USA
SOURCE: Protides Biol. Fluids (1985), Volume Date 1984, 32, 25-9
CODEN: PBFPA6; ISSN: 0079-7065
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 33 refs. **IgA antibodies** produced by plasma cells distributed in secretory tissues assocd. with mucosal surfaces represent a major host defense against environmental antigens. Animal studies have shown that precursors of these IgA cells originate in gut-assocd. lymphoreticular tissues which contain a high frequency of IgA-committed B cells. Antigen-sensitized cells migrate to the blood circulation and home to various mucosal sites. Evidence for the existence of such a common mucosal system in humans is supported by the following findings: a) secretions from glands not directly stimulated with microbial and food antigens contain natural **antibodies**; b) a secretory **IgA** response in such secretions can be artificially induced by the oral **administration** of killed or live microbial vaccines and food antigens; and c) human peripheral blood lymphocytes stimulated with various mitogens produce predominantly polymeric **IgA** (principal form of **IgA** in external secretions) and display an equal distribution of IgA1 and IgA2 cells which is characteristic of external secretory tissues.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 09:26:38 ON 26 FEB 2002)
L5 164 S L4

L6 35 S L5 AND (PARENTERAL? OR INJECT?)

L9 29 DUP REM L6 (6 DUPLICATES REMOVED)

L9 ANSWER 1 OF 29 MEDLINE
ACCESSION NUMBER: 2002076988 IN-PROCESS
DOCUMENT NUMBER: 21662154 PubMed ID: 11803067
TITLE: Oxidised mannan as a novel adjuvant inducing mucosal IgA production.
AUTHOR: Stambas John; Pietersz Geoffrey; McKenzie Ian; Cheers Christina
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Melbourne, 3052, Vic., Parkville, Australia.
SOURCE: VACCINE, (2002 Jan 15) 20 (7-8) 1068-78.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020125

AB Mannan, oxidatively coupled to recombinant protein antigens, has here been tested as a possible adjuvant for the production of **antibody** on the mucosa. Given intranasally, but not intraperitoneally, mannan markedly enhanced the production of **IgA**, IgG1 and IgG2a in the serum, and **IgA** locally in the lung and at remote mucosal sites, including tears, vaginal and salivary secretions. Oxidative coupling was critical to its action, since neither mannan simply mixed with protein nor mannan-protein conjugates which had been reduced by treatment with sodium borohydride, acted as adjuvants. Oxidatively coupled mannan was compared with the widely studied mucosal adjuvant, cholera toxin (CT). The use of oxidised mannan as an adjuvant induced better responses than CT judged by the induction of **IgA** in serum, vaginal washings and saliva. Thus, oxidised mannan, which is non-toxic and can be **administered** without **injection**, is a suitable adjuvant coupled with protective antigens for vaccinating against a number of infections that occur via the **mucous membranes**.

L9 ANSWER 2 OF 29 MEDLINE
ACCESSION NUMBER: 2000340885 MEDLINE
DOCUMENT NUMBER: 20340885 PubMed ID: 10878493
TITLE: Transmission of **IgA** and **IgG** monoclonal **antibodies** to mucosal fluids following intranasal or **parenteral** delivery.
AUTHOR: Falero-Diaz G; Challacombe S; Rahman D; Mistry M; Douce G; Dougan G; Acosta A; Ivanyi J
CORPORATE SOURCE: Department of Oral Medicine and Pathology, GKT School of Medicine and Dentistry Guy's Hospital, London, UK.
SOURCE: INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (2000 Jun) 122 (2) 143-50.
Journal code: BJ7; 9211652. ISSN: 1018-2438.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000811
Last Updated on STN: 20000811
Entered Medline: 20000803

AB BACKGROUND: The efficacy by which passive **antibodies** can reach the lungs could be important for the outcome of immunotherapy of respiratory pulmonary infections. We examined how transmission to a number of mucosal sites is affected by the route of inoculation. METHODS: Transmission of newly raised **IgA** class Mabs against mycobacterial surface antigens to saliva, lung or vaginal lavage, bile and serum of BALB/c mice was compared with existing **IgG** Mabs. ELISA was used for testing body fluids obtained 1-24 h after intranasal or intravenous inoculation and 1-7 days following back-pack tumour growth of hybridomas. RESULTS: Intranasal inoculation resulted in a rapid rise and high levels of both **IgA** and **IgG** class Mabs in lung lavage. In contrast, following intravenous Mab **injection** or back-pack tumour growth of hybridoma cells, effective lung transmission was observed for the IgG1 and IgG2b MAbs, but not for the **IgA** Mabs. The secretory component was acquired by the transmitted **IgA** MAbs in the mucosal fluids, but not in the serum. Nevertheless, the time course of mucosal **IgA** **antibody** levels was similar to that of the tested **IgG** Mabs. Furthermore, the relative proportion of transmission to saliva and bile varied between individual Mabs indicating a role of tissue-specific, immunoglobulin class-unrelated mechanisms. CONCLUSIONS: Intranasal, rather than **parenteral** inoculation of mice is required for the efficient delivery of **IgA** **antibodies** against respiratory pulmonary pathogens. Interestingly, **IgA**-secretory component complexing of intranasally applied Mabs did not significantly influence their persistence in the lungs.

L9 ANSWER 3 OF 29 MEDLINE
ACCESSION NUMBER: 1999290343 MEDLINE
DOCUMENT NUMBER: 99290343 PubMed ID: 10363675
TITLE: Induction of antibody responses in the common mucosal immune system by respiratory syncytical virus immunostimulating complexes.
AUTHOR: Hu K F; Ekstrom J; Merza M; Lovgren-Bengtsson K; Morein B
CORPORATE SOURCE: Swedish University of Agricultural Sciences, College of Veterinary Medicine, Department of Veterinary Microbiology, Uppsala.. Kefei.Hu@bmc.uu.se
SOURCE: MEDICAL MICROBIOLOGY AND IMMUNOLOGY, (1999 May) 187 (4) 191-8.
Journal code: M58; 0314524. ISSN: 0300-8584.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990816
Last Updated on STN: 19990816
Entered Medline: 19990804

AB Immunostimulating complexes (ISCOMs) containing envelope proteins of respiratory syncytial virus (RSV) were explored as a mucosal

delivery system for the capacity of inducing a common mucosal **antibody** response. Two intranasal (i.n.) **administrations** of BALB/c mice with ISCOMs induced potent serum **IgG**, and strong **IgA** responses to RSV locally in the lungs and the upper respiratory, and remotely in the genital and the intestinal tracts. Virtually no measurable **IgA** response was found in these mucosal organs after two subcutaneous (s.c.) immunizations. Virus neutralizing (VN) **antibodies** were detected in serum and in all of the mucosal organ extracts after both s.c. and i.n. immunizations indicating that the neutralizing epitopes were preserved after both mucosal and **parenteral** modes of **administration**. While the mucosal **IgA** response appears to be of mucosal origin, the **IgG antibodies** to RSV detected in the mucosal organs were likely of serum origin. However, the mucosal VN **antibodies** correlated with the **IgG** rather than the **IgA** levels. An enhanced IgA response to gp120 in various mucosal organs was recorded after i.n. immunization with gp120 incorporated in RSV ISCOMs, indicating a role of RSV envelope proteins in enhancing and targeting mucosal responses to passenger antigens.

L9 ANSWER 4 OF 29 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1999265127 MEDLINE
DOCUMENT NUMBER: 99265127 PubMed ID: 10332723
TITLE: Otitis media: the chinchilla model.
AUTHOR: Giebink G S
CORPORATE SOURCE: Otitis Media Research Center, University of Minnesota School of Medicine, Minneapolis 55455, USA.
SOURCE: MICROBIAL DRUG RESISTANCE, (1999 Spring) 5 (1) 57-72. Ref: 157
Journal code: CRS; 9508567. ISSN: 1076-6294.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990730
Last Updated on STN: 19990730
Entered Medline: 19990720

AB Streptococcus pneumoniae infection and disease have been modeled in several animal species including infant and adult mice, infant and adult rats, infant Rhesus monkeys, and adolescent and adult chinchillas. Most are models of sepsis arising from intravenous or intraperitoneal inoculation of bacteria, and a few were designed to study disease arising from intranasal infection. Chinchillas provide the only animal model of middle ear pneumococcal infection in which the disease can be produced by very small inocula **injected** into the middle ear (ME) or intranasally, and in which the disease remains localized to the ME in most cases. This model, developed at the University of Minnesota in 1975, has been used to study pneumococcal pathogenesis at a mucosal site, immunogenicity and efficacy of pneumococcal capsular polysaccharide (PS) vaccine antigens, and the kinetics and efficacy of antimicrobial drugs. Pathogenesis experiments in the chinchilla model have revealed variation in ME virulence among different pneumococcal serotypes,

enhancement of ME infection during concurrent intranasal influenza A virus infections, and natural resolution of pneumococcal otitis media (OM) without intervention. Research has explored the relative contribution of pneumococcal and host products to ME inflammation. Pneumococcal cell wall components and pneumolysin have been studied in the model. Host inflammatory responses studied in the chinchilla ME include polymorphonuclear leukocyte oxidative products, hydrolytic enzymes, cytokine and eicosanoid metabolites, and ME epithelial cell adhesion and **mucous** glycoprotein production. Both clinical (tympanic **membrane** appearance) and histopathology (ME, Eustachian tube, inner ear) endpoints can be quantified. Immunologic and inflammatory studies have been facilitated by the production of affinity-purified antichinchilla **immunoglobulin G (IgG)**, **IgM**, and secretory **IgA** polyclonal **antibody** reagents, and the identification of cross-reactivity between human and chinchilla cytokines, and between guinea pig and chinchilla C3. Alteration of ME mucosa by pneumococcal neuraminidase and alteration of ME epithelial cell (MEEC) surface carbohydrates during intranasal pneumococcal infection have been demonstrated. Pathogenesis studies have been aided by cultured chinchilla MEEC systems, in which the ability of platelet activating factor and interleukin (IL)-1 beta to stimulate epithelial mucous glycoprotein synthesis has recently been demonstrated. Because chronic OM with effusion is characterized by presence of large amounts of mucous glycoprotein in the ME, pneumococcus may have an important role in both acute and chronic ME disease. Both unconjugated PS and PS-protein-conjugated vaccines are immunogenic after intramuscular **administration** without adjuvant in chinchillas. Passive protection studies with human hyperimmune immunoglobulin demonstrated that anti-PS **IgG** alone is capable of protecting the chinchilla ME from direct ME challenge with pneumococci. Active PS immunization studies demonstrated protection following direct ME and intranasal pneumococcal challenge with and without concurrent influenza A virus infection. An attenuated influenza A virus vaccine also showed protection for pneumococcal OM. Antimicrobial treatment of acute OM has been based almost exclusively on empirical drug use and clinical trials without a foundation of ME pharmacokinetics. Studies in the chinchilla model have started to bring a rational basis to drug selection and dosing. Microassays have been developed using high-pressure liquid chromatography for many relevant drugs. Studies have explored the in vivo ME response in pneumococcal OM to antimicrobial drugs at supra- and sub-minimum inhibitory concentration (MIC), the effect of concurrent influenza A virus infection on ME drug penetration, and the effect of treatment on sensorineural hearing loss produced by pneumococcal OM.

L9 ANSWER 5 OF 29 MEDLINE
ACCESSION NUMBER: 1999043920 MEDLINE
DOCUMENT NUMBER: 99043920 PubMed ID: 9826370
TITLE: Specific-antibody-secreting cells in the rectums and genital tracts of nonhuman primates following vaccination.
AUTHOR: Eriksson K; Quiding-Jarbrink M; Osek J; Moller A; Bjork S; Holmgren J; Czerkinsky C
CORPORATE SOURCE: Department of Medical Microbiology and Immunology, University of G oteborg, Goteborg, Sweden.. Kristina.Eriksson@microbio.gu.se

CONTRACT NUMBER: 1 RO1 A135543-02
SOURCE: INFECTION AND IMMUNITY, (1998 Dec) 66 (12) 5889-96.
Journal code: GO7; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981224

AB To determine optimal strategies to induce specific-**antibody**-secreting cells (specific ASC) in the rectal and vaginal mucosae, we immunized monkeys with a prototype mucosal immunogen, cholera toxin (CT), given locally or via gastric or **parenteral administration**. Repeated rectal or vaginal CT immunizations induced strong mucosal and systemic ASC responses. The mucosal responses were, however, confined to the immunization sites and comprised high levels of both specific antitoxin **immunoglobulin A** (**IgA**) and **IgG**. Large numbers of specific **IgA** and **IgG** ASC were detected in cell suspensions from dissociated genital and rectal tissues, demonstrating local accumulation of effector **B cells** at these sites. Intragastric immunization with CT did not per se give rise to cervicovaginal or rectal ASC responses but did prime for a rectal **IgA** ASC response to local booster immunization. Both rectal and vaginal immunizations also induced circulating blood **IgG** ASC and **IgA** ASC. In conclusion, these results show that local **administration** of antigen to the rectal or vaginal mucosa results in higher ASC responses than systemic or distant mucosal delivery. Furthermore, both the vaginal and the rectal mucosae can serve as inductive sites for systemic ASC responses. These observations should be relevant to the development of vaccines against sexually transmitted diseases such as that caused by human immunodeficiency virus.

L9 ANSWER 6 OF 29 MEDLINE

ACCESSION NUMBER: 1998382073 MEDLINE
DOCUMENT NUMBER: 98382073 PubMed ID: 9717973
TITLE: The immunostimulating complex (ISCOM) is an efficient mucosal delivery system for respiratory syncytial virus (RSV) envelope antigens inducing high local and systemic antibody responses.
AUTHOR: Hu K F; Elvander M; Merza M; Akerblom L; Brandenburg A; Morein B
CORPORATE SOURCE: Department of Veterinary Microbiology, College of Veterinary Medicine, Swedish University of Agricultural Sciences, Uppsala.
SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1998 Aug) 113 (2) 235-43.
Journal code: DD7; 0057202. ISSN: 0009-9104.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980917
Last Updated on STN: 19980917

Entered Medline: 19980909

AB ISCOM is an efficient mucosal delivery system for RSV envelope proteins as measured by **antibody** responses in respiratory tract secretions and in sera of mice following two intranasal (i.n.) **administrations**. Intranasally **administered** RSV ISCOMs induced high levels of **IgA antibodies** both in the upper respiratory tract and in the lungs. In the lungs, a prominent and long-lasting **IgA** response was recorded, which still persisted 22 weeks after the second i.n. immunization when the experiment ended. Subcutaneous (s.c.) immunization only induced low **IgA** titres in the upper respiratory tract and no measurable response to RSV was found in the lungs. Differences were also noticed in serum between the i.n. and s.c. modes of immunization. ISCOMs given intranasally induced earlier, higher and longer lasting **IgM** and IgG1 serum anti-RSV **antibody** responses than those induced by the s.c. mode of **administration**. A low serum IgE response was only detectable at 2 weeks after i.n. immunization with ISCOMs and after s.c. immunization with an inactivated virus, but no IgE response was detectable after s.c. **injection** of ISCOMs. The serum **IgA** response was more pronounced following s.c. **injection** of inactivated virus than after i.n. application of ISCOMs, and a clear-cut booster effect was obtained with a second immunization. Virtually no serum **IgA** response was detected after the s.c. **administration** of ISCOMs. In conclusion, the high immune responses induced by RSV ISCOMs in the respiratory tract and serum after i.n. **administration** indicate prominent mucosal delivery and adjuvant properties of the ISCOMs, warranting further studies.

L9 ANSWER 7 OF 29 MEDLINE

ACCESSION NUMBER:	1998148503 MEDLINE
DOCUMENT NUMBER:	98148503 PubMed ID: 9487523
TITLE:	Topical antibody delivery systems produce sustained levels in mucosal tissue and blood.
COMMENT:	Comment in: Nat Biotechnol. 1998 Feb;16(2):136-7
AUTHOR:	Kuo P Y; Sherwood J K; Saltzman W M
CORPORATE SOURCE:	School of Chemical Engineering, Cornell University, Ithaca, NY 14853, USA.
CONTRACT NUMBER:	GM43873 (NIGMS)
SOURCE:	NATURE BIOTECHNOLOGY, (1998 Feb) 16 (2) 163-7. Journal code: CQ3; 9604648. ISSN: 1087-0156.
PUB. COUNTRY:	United States Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	199804
ENTRY DATE:	Entered STN: 19980422 Last Updated on STN: 19980422 Entered Medline: 19980414

AB Immunity at mucosal surfaces, which are ports of entry for many pathogens, is essential in preventing infections. But most current strategies for passive immunization involve **injection** of **antibodies** for systemic, not mucosal, protection. We measured mucosal and systemic **antibody** levels after controlled topical delivery to the vagina. Poly(ethylene-co-vinyl acetate) disks containing 125I-labeled monoclonal **IgG** or anti-lactate dehydrogenase-C4 **antibodies** were placed in

the vaginas of mice. High **antibody** levels (0.26-12 micrograms/ml) were maintained at the mucosal surface for 7 days after disk insertion. **Antibody** molecules also penetrated into the vaginal epithelium, presumably by diffusing through the extracellular space, and entered the circulation. Biologically active **antibodies** were detected in the blood. The **antibody** concentration in the blood was approximately 1% of the concentration in the vagina. Although the permeability of the epithelium to macro-molecules is low, high concentrations were maintained at the luminal surface for an extended period, permitting substantial systemic uptake of **antibody**.

L9 ANSWER 8 OF 29 MEDLINE
ACCESSION NUMBER: 97403056 MEDLINE
DOCUMENT NUMBER: 97403056 PubMed ID: 9258425
TITLE: Serum and mucosal antibody responses and protection in pigs vaccinated against Mycoplasma hyopneumoniae with vaccines containing a denatured membrane antigen pool and adjuvant.
AUTHOR: Djordjevic S P; Eamens G J; Romalis L F; Nicholls P J; Taylor V; Chin J
CORPORATE SOURCE: NSW Agriculture, Elizabeth Macarthur Agricultural Institute, Camden, New South Wales.
SOURCE: AUSTRALIAN VETERINARY JOURNAL, (1997 Jul) 75 (7) 504-11.
Journal code: 9IE; 0370616. ISSN: 0005-0423.
PUB. COUNTRY: Australia
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971209

AB OBJECTIVE: To investigate the protective efficacy of a pool of denatured membrane protein antigens of Mycoplasma hyopneumoniae (J strain) in the molecular size range 70 to 85 kDa (F3 antigen) in combination with adjuvants for pigs challenged with M hyopneumoniae. DESIGN: A vaccine efficacy experiment with assessment of serum and respiratory tract **antibody** responses. PROCEDURE: F3 antigens were emulsified with five different adjuvants. To groups of three pigs per vaccine, four vaccines were given by intramuscular **injection**, and two vaccines, including one of those given intramuscularly, were given by intraperitoneal **injection**. RESULTS: Compared to six unvaccinated pigs, animals vaccinated with F3 antigen displayed significantly reduced pneumonia (54% reduction in mean lung score) following experimental challenge. Analysis of post-vaccination, pre-challenge **IgG** and **IgA** ELISA **antibody** absorbances in serum and respiratory tract washings revealed no correlation with lung score. Six weeks after challenge, pigs previously vaccinated intramuscularly mostly demonstrated greater **IgG** and **IgA** responses in respiratory tract washings, and greater **IgG** serum **antibody** responses, than those vaccinated by intraperitoneal **injection**. CONCLUSION: Pigs vaccinated with M hyponeumoniae antigens in the molecular size range of 70 to 85 kDa showed a significant reduction in lung lesions compared with unvaccinated control animals after experimental challenge. **IgG** and

IgA antibody concentrations in serum and respiratory tract washings after vaccination do not provide a useful prognostic indicator of protection from enzootic pneumonia.

L9 ANSWER 9 OF 29 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 97142860 MEDLINE
DOCUMENT NUMBER: 97142860 PubMed ID: 8988882
TITLE: Novel adjuvants and vaccine delivery systems.
AUTHOR: Morein B; Villacres-Eriksson M; Sjolander A; Bengtsson K L
CORPORATE SOURCE: Swedish University of Agricultural Sciences, Uppsala, Sweden.
SOURCE: VETERINARY IMMUNOLOGY AND IMMUNOPATHOLOGY, (1996 Nov) 54 (1-4) 373-84.
Journal code: XCB; 8002006. ISSN: 0165-2427.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970414
Last Updated on STN: 19970414
Entered Medline: 19970401

AB Conventionally the efficiency of an adjuvant is measured by the capacity to induce enhanced **antibody** serum titres and cell mediated immunity (CMI) to a given antigen. Nowadays the capacity of an adjuvant is also measured by the quality as well as the magnitude of the induced immune response, guided by the protective immune response required. Quality includes isotype and **IgG** subclass responses, T-helper cell responses characterized by the cytokine profile and cytotoxic T cells (CTL). In the early phase of immunization some adjuvants influence the antigen **administration** and uptake by a so-called depot effect exemplified by aluminium hydroxide gel and oil adjuvants, which possibly is not as desired as alledged. A modern depot is exerted by slow release formulations continuously releasing the antigen over a period of time or by pulses at intervals aiming at 'single **injection**' vaccine. Great efforts are made to formulate efficient delivery formulations targeting the antigens from the site of **administration**, to draining lymph nodes or distant lymphatic tissue or to mucosal surfaces by **parenteral** or mucosal **administrations**. Nowadays, non-replicating carriers besides replicating vaccines are formulated to induce mucosal immune responses encompassing secretory **IgA** and CMI. Efforts to evoke immune responses on **mucosal membranes** distant from the site of **administration** have resulted mostly in little success. For a long time it was considered that CTL under the restriction of MHC Class I only could be evoked by replicating viruses or intracellular parasites. However, novel adjuvant delivery systems readily induce CTL by delivering the antigen to the APC resulting in intracellular transport to the cytosol for the MHC Class I presentation system, as well as to the endosomal pathway for the MHC Class II presentation.

L9 ANSWER 10 OF 29 MEDLINE
ACCESSION NUMBER: 94378711 MEDLINE
DOCUMENT NUMBER: 94378711 PubMed ID: 8091852
TITLE: Induction of local and systemic immunity against

human respiratory syncytial virus using a chimeric FG glycoprotein and cholera toxin B subunit.
AUTHOR: Oien N L; Brideau R J; Walsh E E; Wathen M W
CORPORATE SOURCE: Department of Cancer and Infectious Diseases, Upjohn Company, Kalamazoo, MI 49001.
SOURCE: VACCINE, (1994 Jun) 12 (8) 731-5.
Journal code: X60; 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941031
Last Updated on STN: 19941031
Entered Medline: 19941020

AB Local **IgA** and **IgG antibodies** against respiratory syncytial virus (RSV) were induced in the respiratory tract of mice following intranasal vaccination with an RSV chimeric FG glycoprotein and cholera toxin B (CTB) as a mucosal adjuvant. Local **antibody** production was not induced following **parenteral** immunization with FG **administered** in alum adjuvant. While both vaccination protocols induced serum **antibodies** against RSV and protected the lower respiratory tract from RSV infection, only intranasal FG/CTB afforded protection of the upper respiratory tract. These data suggest that vaccination via the mucosal route may be superior to vaccination by a parental route in providing complete protection against RSV.

L9 ANSWER 11 OF 29 MEDLINE
ACCESSION NUMBER: 94131572 MEDLINE
DOCUMENT NUMBER: 94131572 PubMed ID: 7507892
TITLE: Local immune response and protection in the guinea pig keratoconjunctivitis model following immunization with Shigella vaccines.
AUTHOR: Hartman A B; Van de Verg L L; Collins H H Jr; Tang D B; Bendiuk N O; Taylor D N; Powell C J
CORPORATE SOURCE: Department of Enteric Infections, Walter Reed Army Institute of Research, Washington, D.C. 20307-5100.
SOURCE: INFECTION AND IMMUNITY, (1994 Feb) 62 (2) 412-20.
Journal code: GO7; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940318
Last Updated on STN: 19960129
Entered Medline: 19940304

AB This study used the guinea pig keratoconjunctivitis model to examine the importance of route of **administration** (mucosal versus **parenteral**), frequency and timing of immunization (primary versus boosting immunization), and form of antigen given (live attenuated vaccine strain versus O-antigen-protein conjugate) on the production of protective immunity against Shigella infection. Since local immune response to the lipopolysaccharide (LPS) O-antigen of Shigella spp. is thought to be important for protection against disease, O-antigen-specific **antibody**-secreting cells (ASC) in the spleen and regional lymph nodes of immunized animals were

measured by using an ELISPOT assay. Results indicated that protective efficacy was associated with a strong O-antigen-specific ASC response, particularly in the superficial ventral cervical lymph nodes draining the conjunctivae. In naive animals, a strong ASC response in the cervical lymph nodes and protection against challenge were detected only in animals that received a mucosal immunization. Protection in these animals was increased by a boosting mucosal immunization. While **parenteral** immunization alone with an O-antigen-protein conjugate vaccine did not protect naive animals against challenge, a combined **parenteral**-mucosal regimen elicited enhanced protection without the addition of a boosting immunization. Although O-antigen-specific serum **immunoglobulin A** titers were significantly higher in animals receiving a mucosal immunization, there was no apparent correlation between levels of serum **antibody** and protection against disease.

L9 ANSWER 12 OF 29 MEDLINE
ACCESSION NUMBER: 95046935 MEDLINE
DOCUMENT NUMBER: 95046935 PubMed ID: 7958476
TITLE: Mucosal vaccines based on the use of cholera toxin B subunit as immunogen and antigen carrier.
AUTHOR: Lebens M; Holmgren J
CORPORATE SOURCE: Department of Medical Microbiology and Immunology, University of Goteborg, Sweden.
SOURCE: DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, (1994) 82 215-27. Ref: 39
Journal code: E7V; 0427140. ISSN: 0301-5149.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 19950110
Entered Medline: 19941221

AB Stimulation of strong mucosal **IgA** immune responses as a basis for vaccine-induced protection against various pathogens has proved difficult. Most soluble protein antigens **administered** either **parenterally** or oral-mucosally have given disappointing results. A notable exception in this regard are cholera toxin (CT) and, particularly in humans, its non-toxic B subunit pentamer moiety (CTB) both of which stimulate a strong intestinal **IgA antibody** response and long-lasting immunological memory. Based on this, CTB has become an important component in recently developed oral vaccines against cholera and diarrhea caused by enterotoxigenic E. coli. The strong immunogenicity of CT and CTB can to a large extent be explained by their ability to bind to receptors on the intestinal mucosal surface. This has promoted much recent interest in the use of CTB as an oral delivery carrier for other vaccine-relevant antigens. Oral **administration** of antigens coupled to CTB either chemically or genetically has in several systems been found to markedly potentiate both intestinal and extra-intestinal **IgA** immune responses against the CTB-coupled antigens and to elicit substantial circulating **antibody** responses. In contrast to CTB, CT

also has strong adjuvant properties for stimulating mucosal **IgA** immune responses to unrelated, non-coupled antigens after oral co-immunization. This adjuvant activity appears to be closely linked to the A subunit-catalyzed ADP-ribosylating action of CT leading to enhanced cyclic AMP formation in the affected cells.

L9 ANSWER 13 OF 29 MEDLINE
ACCESSION NUMBER: 94273030 MEDLINE
DOCUMENT NUMBER: 94273030 PubMed ID: 8004535
TITLE: Immune response of heifers to vaginal submucosal or subcutaneous vaccination and intravaginal challenge with Ureaplasma diversum.
AUTHOR: Mulira G L; Saunders J R
CORPORATE SOURCE: Department of Veterinary Microbiology, Western College of Veterinary Medicine, University of Saskatchewan, Saskatoon.
SOURCE: CANADIAN JOURNAL OF VETERINARY RESEARCH, (1994 Apr) 58 (2) 109-13.
Journal code: CKL; 8607793. ISSN: 0830-9000.
PUB. COUNTRY: Canada
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 19940729
Last Updated on STN: 19970203
Entered Medline: 19940719

AB Twenty beef heifers were randomly assigned to five equal groups and vaccinated: Group 1--in vaginal submucosa (VM) with Ureaplasma diversum ultrasonicated whole cells (WC) in complete Freund's adjuvant (CFA); Group 2--in VM with U. diversum cell membranes (CM) in CFA; Group 3--subcutaneously (SC) with CM in CFA; Group 4--in VM with CM alone; and Group 5--in VM with phosphate buffered saline (PBS) in CFA. A second vaccination with the same antigens in incomplete Freund's adjuvant was given after four weeks, and three weeks later, all heifers were challenged intravaginally with 3.6 x 10(7) colony-forming units (CFU) of U. diversum strain 2312. Immunoglobulins that reacted with U. diversum were measured in serum and cervicovaginal mucus (CVM) by an enzyme-linked-immunosorbent assay. In groups 1 and 2, vaccination by the VM route with WC or CM antigens, stimulated high levels of U. diversum-reactive IgG1 and IgG2 **antibodies** in serum as well as CVM, but a low **IgA** response only in CVM. In group 4, VM vaccination with CM (no adjuvant) elicited a minimal IgG1 and IgG2 response in serum and CVM. In group 3, SC vaccination with CM antigen stimulated high IgG1 and IgG2 reactivity in both serum and CVM, but no **IgA** reactivity. Very little **IgM** reactivity was detected in the four vaccinated groups. Intravaginal challenge resulted in characteristic granular vulvitis in all vaccinated and control heifers, with all animals remaining culture-positive for the 35 day observation period. The infection stimulated a marked increase in the specific **IgA** response in CVM of the three groups vaccinated with either, adjuvanted antigen.(ABSTRACT TRUNCATED AT 250 WORDS)

L9 ANSWER 14 OF 29 MEDLINE

ACCESSION NUMBER: 94263008 MEDLINE
DOCUMENT NUMBER: 94263008 PubMed ID: 8203723
TITLE: Strategies for the induction of immune responses at mucosal surfaces making use of cholera toxin B subunit as immunogen, carrier, and adjuvant.
AUTHOR: Holmgren J; Czerkinsky C; Lycke N; Svennerholm A M
CORPORATE SOURCE: Department of Medical Microbiology and Immunology, University of Goteborg, Sweden.
SOURCE: AMERICAN JOURNAL OF TROPICAL MEDICINE AND HYGIENE, (1994) 50 (5 Suppl) 42-54. Ref: 65
Journal code: 3ZQ; 0370507. ISSN: 0002-9637.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 19940714
Last Updated on STN: 19940714
Entered Medline: 19940705

AB The concept of a common mucosal immune system, through which specific antigen-activated lymphocytes from the gut can disseminate immunity both along the intestinal tract and to various other mucosal and glandular tissues, has generated much current interest in the possibility of developing oral vaccines, not only for enteric infections but also for infections in the respiratory and urogenital tracts. However, to date it has proven difficult in practice to stimulate strong mucosal **IgA** immune responses by either **parenteral** or oral-mucosal **administration** of most antigens, and experience with soluble protein antigens has, on the whole, been disappointing. A notable exception in this regard is cholera toxin (CT) and in humans more than in other species, its nontoxic B subunit pentamer moiety (CTB). Based on this, CTB has become an important component in recently developed oral vaccines against cholera as well as against diarrhea caused by enterotoxigenic Escherichia coli producing CT-like heat-labile enterotoxin(s). Since the strong immunogenicity of CT and CTB can, to a large extent, be explained by their ability to bind to receptors on the intestinal mucosal surface, there has recently been much interest in approaches using CTB as an oral delivery carrier system for other vaccine-relevant antigens, and much progress has been made in preparing immunogenic hybrid proteins by coupling various protein or peptide antigens chemically or genetically to CTB. Indeed, in several systems, oral **administration** of such hybrid antigens has been found to markedly potentiate both intestinal and extraintestinal **IgA** immune responses against the CTB-coupled antigens and also to elicit substantial circulating **antibody** responses. Besides the mucosal immunopotentiating effect of either CT or CTB owing to their similar capacity as oral antigen-delivery vehicles, CT, but in most systems tested not CTB, also has strong adjuvant properties for stimulating mucosal **IgA** immune responses to admixed (not coupled) unrelated antigens after oral immunization. This adjuvant activity appears to be closely linked to the ADP-ribosylating action of CT (and specifically of its A subunit) leading to enhanced cyclic AMP formation in the affected cell, and efforts to eliminate the enterotoxic activity without losing adjuvanticity have so far not

met with success.

L9 ANSWER 15 OF 29 MEDLINE
ACCESSION NUMBER: 93122829 MEDLINE
DOCUMENT NUMBER: 93122829 PubMed ID: 1478688
TITLE: Antibody-secreting cell responses in the mouse liver.
AUTHOR: Wu H Y; Russell M W
CORPORATE SOURCE: Department of Microbiology, University of Alabama, Birmingham 35294.
CONTRACT NUMBER: DE-06746 (NIDCR)
DK-28537 (NIDDK)
SOURCE: IMMUNOLOGY, (1992 Nov) 77 (3) 443-8.
Journal code: GH7; 0374672. ISSN: 0019-2805.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199302
ENTRY DATE: Entered STN: 19930226
Last Updated on STN: 20000303
Entered Medline: 19930210

AB To elucidate the origins of biliary **IgA antibodies**, we investigated the isotype and specificity of **antibody**-secreting cells (ASC) in the liver in comparison with the spleen and intestinal lamina propria of mice immunized by peroral or **parenteral** routes. The profile of specific **IgM**, IgG1, IgG2a, and **IgA** ASC in the liver resembled that of the spleen rather than the lamina propria, regardless of the route of immunization. Peroral immunization increased the proportion of specific **IgA** ASC in all three organs. However, liver mononuclear cells (MNC) contained a higher proportion of total **IgA**-secreting cells than spleen cells. After immunization, the number and proportion of B220+ **B cells** were increased in the liver but not in the spleen. Although the predominant isotype of Ig and specific **antibody** in bile in response to immunization by either route was **IgA**, **IgM** and **IgG** were clearly detectable. However, specific activities of biliary **antibodies** relative to total Ig isotype were generally higher than in serum. The predominance of **IgA**-secreting cells in the liver and the large amount of **IgA** secreted in the bile resemble the situation at other secretory sites of the mucosal immune system. However, specific **antibody**-secreting cells appear to accumulate in the liver promptly after immunization, regardless of isotype, and contribute locally produced **antibodies** to the bile.

L9 ANSWER 16 OF 29 MEDLINE
ACCESSION NUMBER: 93198761 MEDLINE
DOCUMENT NUMBER: 93198761 PubMed ID: 1295333
TITLE: Prospects for human mucosal vaccines.
AUTHOR: Mestecky J; McGhee J R
CORPORATE SOURCE: Department of Microbiology, University of Alabama, Birmingham 35294-10005.
CONTRACT NUMBER: AI-15128 (NIAID)
AI-18745 (NIAID)
DE08182 (NIDCR)
SOURCE: ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1992)

327 13-23. Ref: 64
Journal code: 2LU; 0121103. ISSN: 0065-2598.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199304
ENTRY DATE: Entered STN: 19930423
Last Updated on STN: 20000303
Entered Medline: 19930412

AB The selective induction of **antibodies** in external secretions and mucosal T cell-mediated immunity are desirable for the prevention of various systemic as well as predominantly mucosa-restricted infections. An enormous surface area of **mucosal membranes** is protected primarily by **antibodies** that belong, in many species, to the **IgA** isotype. Such **antibodies** are produced locally by large numbers of **IgA**-containing plasma cells distributed in subepithelial spaces of **mucosal membranes** and in the stroma of secretory glands. In humans and in some animal species, plasma-derived **IgA antibodies** do not enter external secretions in significant quantities and systemically **administered** preformed **IgA antibodies** would be of little use for passive immunization. Systemic **administration** of microbial antigens may boost an effective S-**IgA** immune response only in a situation whereby an immunized individual had previously encountered the same antigen by the mucosal route. Immunization routes that involve ingestion or possibly inhalation of antigens lead to the induction of not only local but also generalized immune responses, manifested by the parallel appearance of S-**IgA antibodies** to ingested or inhaled antigens in secretions of glands distant from the site of immunization. Convincing evidence is available that antigen-sensitized and **IgA**-committed precursors of plasma cells and T cells from **IgA** inductive sites (e.g., BALT, GALT, and tonsils) are disseminated to the gut, other mucosa-associated tissues, and exocrine glands. However, due to the limited absorption of desired antigens from the gut lumen of orally immunized individuals, repeated large doses of antigens are required for an effective S-**IgA** response. Novel antigen delivery systems for the stimulation of such responses has been briefly reviewed here. These, of course, include genetically engineered bacteria and viruses, CT/CFB, liposomes and microspheres. Live attenuated or genetically manipulated bacteria expressing other microbial antigens have been used for selective colonization of GALT. Unique antigen packaging and the use of adjuvants suitable for oral **administration** hold promise for an efficient antigen delivery to critical tissues in the intestine and deserve extensive exploration. The oral immunization route appears to have many advantages over systemic immunization; however, one must consider alternate **IgA** inductive sites and compartmentalization within the Common Mucosal Immune System. In addition to providing immunity on mucosal surfaces, which are the most common sites of entry of infectious agents, the mucosal routes of **administration** are more acceptable and do not require stringent criteria applicable for **injectable** vaccines,

storage problems may be simplified, and large populations of individuals can be immunized simultaneously without the assistance of highly trained health personnel.

L9 ANSWER 17 OF 29 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92012172 EMBASE
DOCUMENT NUMBER: 1992012172
TITLE: [**Mucosal** immunization with an outer-**membrane**-protein (OMP)-vaccine of P. aeruginosa].
LOKALE IMMUNISIERUNG GEGEN P. AERUGINOSA MIT EINER OUTER-MEMBRANE-PROTEIN (OMP)-VAKZINE.
AUTHOR: Grundmann T.; Freihorst J.; Kubesch P.; Tummler B.; Von Der Hardt H.
CORPORATE SOURCE: Abt. Kinderheilkunde I, Medizinische Hochschule, Konstanty-Gutschow-Str. 8, 3000 Hannover 61, Germany
SOURCE: Pneumologie, (1991) 45/11 (924-927).
ISSN: 0934-8387 CODEN: PNEMEC
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: German
SUMMARY LANGUAGE: English; German
AB Averting initial colonization of the respiratory tract with P. aeruginosa would be of great benefit for patients with cystic fibrosis (CF). Our approach to this problem is mucosal immunization with a vaccine prepared from the OMP fraction of a PAO-1 strain of P. aeruginosa. Sprague-Dawley rats were given 5 intragastric doses of the vaccine on 5 consecutive days and an intranasal booster dose 21 days later. Immunized animals developed high titers of OMP-specific **IgG antibodies** in serum and a specific **IgA**-response in bronchioalveolar and small intestinal lavage samples, all determined by ELISA. When challenged 7 days after the booster (day 28) by intratracheal **injection** of live bacteria of a heterologous strain of P. aeruginosa the immunized rats showed enhanced bronchopulmonary bacterial clearance compared to nonimmunized controls, as indicated by bacterial counts from homogenized lung tissue taken 4 hrs after challenge. Thus, mucosal immunization with OMP vaccines might hinder initial colonisation of the lungs with P. aeruginosa.

L9 ANSWER 18 OF 29 MEDLINE
ACCESSION NUMBER: 90256281 MEDLINE
DOCUMENT NUMBER: 90256281 PubMed ID: 2341186
TITLE: Liposomes containing anti-idiotypic antibodies: an oral vaccine to induce protective secretory immune responses specific for pathogens of mucosal surfaces.
AUTHOR: Jackson S; Mestecky J; Childers N K; Michalek S M
CORPORATE SOURCE: Department of Microbiology, University of Alabama, Birmingham 35294.
CONTRACT NUMBER: DE 00155 (NIDCR)
DE 08182 (NIDCR)
DE 08228 (NIDCR)
+

SOURCE: INFECTION AND IMMUNITY, (1990 Jun) 58 (6) 1932-6.
Journal code: GO7; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199006
ENTRY DATE: Entered STN: 19900720
Last Updated on STN: 20000303
Entered Medline: 19900625

AB By using a gnotobiotic rat model system to study the induction of protective immune responses by anti-idiotype (anti-id) vaccines specific for **antibodies** directed at the cariogenic microorganism Streptococcus mutans, it was shown that **administration** of such an anti-id vaccine provided partial protection against dental caries after challenge with virulent microorganisms. Protective effects were first demonstrated by direct **parenteral administration** of the anti-id vaccine into salivary gland regions, as determined by reductions in microbial colonization and caries scores. Subsequently, the anti-id was incorporated into liposomes and **administered** by gastric intubation. Immunization by this regimen also resulted in a significant reduction in caries as well as S. mutans colonization of the oral cavity, with concomitant increases in salivary **immunoglobulin A** anti-S. mutans **antibodies** . These data provide evidence that anti-id vaccines specifically targeted at the secretory immune system can induce protective immune responses to pathogens of mucosal surfaces.

L9 ANSWER 19 OF 29 MEDLINE

ACCESSION NUMBER: 90110997 MEDLINE
DOCUMENT NUMBER: 90110997 PubMed ID: 2295788
TITLE: Glucocorticoid regulation of the humoral immune system. I. In vivo effects of dexamethasone on IgA and IgG in serum and at mucosal surfaces.
AUTHOR: Wira C R; Sandoe C P; Steele M G
CORPORATE SOURCE: Department of Physiology, Dartmouth Medical School, Hanover, NH 03756.
CONTRACT NUMBER: AI 13541 (NIAID)
SOURCE: JOURNAL OF IMMUNOLOGY, (1990 Jan 1) 144 (1) 142-6.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199002
ENTRY DATE: Entered STN: 19900328
Last Updated on STN: 19900328
Entered Medline: 19900209

AB The present studies were undertaken to determine whether glucocorticoids influence the levels of Ig in serum, saliva, and vaginal secretions. When measured by RIA, **IgA** levels in serum were elevated when increasing doses of dexamethasone, a potent synthetic glucocorticoid, were **administered** to intact- and adrenalectomized-ovariectomized rats. In contrast, **IgA** levels decreased in saliva and vaginal secretions over the same dose range. Time course studies indicated that the decline in salivary **IgA**, observed at 24 h after a single **injection** of

dexamethasone, preceded a rise in serum **IgA** detected at 24 h after the second hormone treatment. Both responses were maximal at day 2 and did not change with further hormone exposure. After immunization and boosting with SRBC at two mucosal sites (intestinal Peyer's patch and uterine lumen), dexamethasone increased anti-SRBC **IgA antibody** levels in serum and reduced their presence in vaginal secretions. In contrast, anti-SRBC **IgG -antibody** levels in serum and vaginal secretions were reduced with hormone treatment. In the absence of hormone treatment, pooled sera from nonimmunized animals, when analyzed by HPLC, contained polymeric and dimeric **IgA** that was present in roughly equal proportion. In response to dexamethasone, polymeric **IgA** increased to a greater extent than did monomeric **IgA**. In summary, these studies demonstrate that dexamethasone alters the levels of **IgA** as well as specifically directed **IgA** and **IgG antibodies** in secretions and serum. Further, it suggests that glucocorticoid controlled **IgA** increases in serum and decreases in vaginal and salivary secretions may be due, in part, to a redistribution of polymeric **IgA** from mucosal surfaces to serum.

L9 ANSWER 20 OF 29 MEDLINE
ACCESSION NUMBER: 89339709 MEDLINE
DOCUMENT NUMBER: 89339709 PubMed ID: 2668182
TITLE: Difference between bacterial and food antigens in mucosal immunogenicity.
AUTHOR: Wold A E; Dahlgren U I; Hanson L A; Mattsby-Baltzer I; Midvetdt T
CORPORATE SOURCE: Department of Clinical Immunology, University of Goteborg, Sweden.
SOURCE: INFECTION AND IMMUNITY, (1989 Sep) 57 (9) 2666-73. Journal code: GO7; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198909
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19890915

AB The mucosa-associated lymphoid tissue may deviate from its systemic counterpart in being able to discriminate between microbial and nonmicrobial antigens. To study this, the systemic and mucosal **antibody** responses to bacterial and food antigens were followed in parallel in female rats during two pregnancies and lactation periods. Germfree rats were monocolonized with an Escherichia coli O6K13H1 strain, and their diet was switched to pellets containing large amounts of ovalbumin and beta-lactoglobulin. **Antibodies** against O6 lipopolysaccharide already appeared in serum and bile 1 week after colonization, and those against type 1 fimbriae appeared a few weeks later. Serum **immunoglobulin G antibodies** against the E. coli enzyme beta-galactosidase were found in moderate titers in all rats after 16 weeks of exposure. In contrast, few rats had detectable **antibody** levels against the dietary proteins ovalbumin and beta-lactoglobulin in serum or bile even after 16 weeks of exposure. In the milk, **antibodies**

against E. coli beta-galactosidase and type 1 fimbriae reached the highest titers, while moderate titers were found against the food antigens and against O6 lipopolysaccharide. The difference in immune reactivity against bacterial versus dietary antigens was not likely due to insufficient amounts of the latter reaching lymphoid tissue, since (i) uptake studies indicated that ovalbumin was more efficiently taken up than endotoxin and (ii) the same difference in antigenicity between ovalbumin and E. coli was seen after immunization directly into Peyer's patches. We therefore suggest that a prerequisite for a strong mucosal **antibody** response is that the antigen be encountered by the gut-associated lymphoid tissue within microorganisms capable of stimulating antigen presentation.

L9 ANSWER 21 OF 29 MEDLINE
ACCESSION NUMBER: 90373706 MEDLINE
DOCUMENT NUMBER: 90373706 PubMed ID: 2561961
TITLE: Cholera toxin as a mucosal adjuvant for respiratory antibody responses in mice.
AUTHOR: Liang X P; Lamm M E; Nedrud J G
CORPORATE SOURCE: Institute of Pathology, Case Western Reserve University, Cleveland, OH 44106.
CONTRACT NUMBER: AI26449 (NIAID)
HL37117 (NHLBI)
SOURCE: REGIONAL IMMUNOLOGY, (1989 Jul-Aug) 2 (4) 244-8.
Journal code: AVT; 9001013. ISSN: 0896-0623.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199010
ENTRY DATE: Entered STN: 19901122
Last Updated on STN: 19970203
Entered Medline: 19901015

AB Cholera toxin was investigated as an adjuvant for anti-virus **antibody** responses in the respiratory mucosa of mice. Two methods of applying cholera toxin were evaluated: oral **administration** and intranasal **administration**. Oral immunization with Sendai virus in the presence of cholera toxin effectively primed for respiratory anti-viral **antibody** responses, whereas oral immunization with Sendai virus alone was ineffective in this respect. In nasal washes, **IgA** was the predominant anti-viral **antibody** enhanced by oral cholera toxin; in bronchoalveolar washes, the enhanced anti-viral **antibodies** included **IgG**, **IgA**, and **IgM**. Effects of direct **administration** of cholera toxin to the respiratory mucosa on respiratory anti-viral **antibody** responses depended on the method of anesthesia used during immunization. With inhalation anesthesia (ether), cholera toxin had no adjuvant effect on respiratory **antibody** responses to coadministered Sendai virus. In contrast, under **parenteral** anesthesia (i.e., intraperitoneal ketamine), mice which received cholera toxin and Sendai virus via the respiratory tract showed significantly higher anti-viral **IgA** and **IgG antibody** titers in nasal washes and **IgG antibody** in bronchoalveolar washes than mice which received the virus only.

L9 ANSWER 22 OF 29 MEDLINE
ACCESSION NUMBER: 90119144 MEDLINE
DOCUMENT NUMBER: 90119144 PubMed ID: 2610110
TITLE: Vaccine-containing biodegradable microspheres specifically enter the gut-associated lymphoid tissue following oral **administration** and induce a disseminated mucosal immune response.
AUTHOR: Eldridge J H; Meulbroek J A; Staas J K; Tice T R; Gilley R M
CORPORATE SOURCE: Department of Microbiology, University of Alabama, Birmingham 35294.
CONTRACT NUMBER: AI 21774 (NIAID)
AI 24772 (NIAID)
SOURCE: ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1989) 251 191-202.
Journal code: 2LU; 0121103. ISSN: 0065-2598.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199002
ENTRY DATE: Entered STN: 19900328
Last Updated on STN: 19970203
Entered Medline: 19900220

AB Biodegradable and biocompatible microspheres have been investigated for their usefulness as a vaccine delivery system for both **parenteral** and enteral immunization. Microspheres composed of poly(DL-lactide-co-glycolide) which contained a toxoid vaccine of Staphylococcal enterotoxin B were found to strongly potentiate the circulating anti-toxin **antibody** response following intraperitoneal **injection**. Following oral **administration**, microspheres less than 10 microns in diameter were specifically taken up into the Peyer's patches of the gut-associated lymphoid tissue, where those greater than or equal to 5 microns remained fixed for an extended period. Microspheres less than 5 microns were disseminated within macrophages to the mesenteric lymph nodes, blood circulation and spleen. Oral immunization with enterotoxoid-containing microspheres induced circulating toxin-specific **antibodies** and a concurrent secretory **IgA** anti-toxin response in saliva, gut wash fluids and bronchial-alveolar wash (BAW) fluids. In contrast, soluble enterotoxoid was completely ineffective as an oral immunogen.

L9 ANSWER 23 OF 29 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 87280584 MEDLINE
DOCUMENT NUMBER: 87280584 PubMed ID: 3301884
TITLE: The common mucosal immune system and current strategies for induction of immune responses in external secretions.
AUTHOR: Mestecky J
CONTRACT NUMBER: AI-18745 (NIAID)
AM-28537 (NIADDK)
SOURCE: JOURNAL OF CLINICAL IMMUNOLOGY, (1987 Jul) 7 (4) 265-76. Ref: 117
Journal code: HRC; 8102137. ISSN: 0271-9142.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198709
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19970203
Entered Medline: 19870910

AB The selective induction of **antibodies** in external secretions is desirable for the prevention of various systemic as well as predominantly mucosa-restricted infections. An enormous surface area of **mucosal membranes** is protected primarily by **antibodies** that belong, in many species, to the **IgA** isotype. Such **antibodies** are produced locally by large numbers of **IgA**-containing plasma cells distributed in subepithelial spaces of **mucosal membranes** and in the stroma of secretory glands. In humans and in some animal species, plasma-derived **IgA antibodies** do not enter external secretions in significant quantities and systemically **administered** preformed **IgA antibodies** would be of little use for passive immunization. Systemic **administration** of microbial antigens may boost an effective S-**IgA** immune response only in a situation whereby an immunized individual had previously encountered the same antigen by the mucosal route. Local **injection** of antigen in the vicinity of secretory glands is usually accompanied by an undesirable concomitant systemic response and frequently requires the addition of adjuvants that are unacceptable for **administration** in humans. Immunization routes that involve ingestion or possibly inhalation of antigens lead to the induction of not only local but also generalized immune responses manifested by the parallel appearance of S-**Iga antibodies** to ingested or inhaled antigens in secretions of glands distant from the site of immunization. Based on extensive studies in animal models as well as in humans, convincing evidence is available that antigen-sensitized and **IgA**-committed precursors of plasma cells from GALT are disseminated to the gut, other mucosa-associated tissues, and exocrine glands. However, due to the limited absorption of desired antigens from the gut lumen of orally immunized individuals, repeated large doses of antigens are required for an effective S-**IgA** response. Novel antigen delivery systems for the stimulation of such responses are currently being examined in several laboratories. Live attenuated or genetically manipulated bacteria expressing other microbial antigens have also been used for selective colonization of gut-associated lymphoid tissues. Unique antigen packaging and the use of adjuvants suitable for oral **administration** hold promise for an efficient antigen delivery to critical tissues in the intestine and deserve extensive exploration. The oral immunization route appears to have many advantages over systemic immunization.(ABSTRACT TRUNCATED AT 400 WORDS)

L9 ANSWER 24 OF 29 MEDLINE
ACCESSION NUMBER: 87040584 MEDLINE
DOCUMENT NUMBER: 87040584 PubMed ID: 3534784
TITLE: [Stevens-Johnson syndrome associated with Mycoplasma pneumoniae infection. Apropos of a pediatric case]. Syndrome de Stevens Johnson associe a une infection a Mycoplasma pneumoniae. A propos d'une observation

pediatrique.
AUTHOR: Lachaux A; Descos B; Rebaud P; Le Gall C; Hermier M
SOURCE: PEDIATRIE, (1986 Apr-May) 41 (3) 221-6.
Journal code: OY8; 0401127. ISSN: 0031-4021.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198612
ENTRY DATE: Entered STN: 19900302
Last Updated on STN: 19900302
Entered Medline: 19861209

AB A 13 years old girl presented an acute episode of fever, productive cough, purulent rhinorrhea and bilateral pulmonary crepitant rales. 36 hours later a maculopapular eruption appeared on the face, extended to all body and became bullous. Pluriorificial **mucous membranes** lesions were associated (conjunctivae, buccal mucosa, lips, nasal mucosa, genitalia and the perirectal area). **Parenteral** prednisone was **administered** and the extension of the eruption was stopped in a few hours. Lesions healed in about 10 days. Association with mycoplasma pneumoniae was documented by serologic studies (high titers of complement fixing **antibodies** and presence of **IgM antibodies** in immunofluorescence).

L9 ANSWER 25 OF 29 MEDLINE
ACCESSION NUMBER: 85029209 MEDLINE
DOCUMENT NUMBER: 85029209 PubMed ID: 6490090
TITLE: Contribution of intraperitoneal immunization to the local immune response in the respiratory tract of sheep.
AUTHOR: Scicchitano R; Husband A J; Clancy R L
SOURCE: IMMUNOLOGY, (1984 Oct) 53 (2) 375-84.
Journal code: GH7; 0374672. ISSN: 0019-2805.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198411
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19841128

AB The contribution of gut-associated lymphoid tissue (GALT) to the local immune response in the respiratory mucosa of sheep has been investigated. Sheep were primed intraperitoneally (i.p.) with antigen in Freund's complete adjuvant, a procedure known to produce a large **IgA**-specific **antibody**-containing cell (ACC) response in intestinal lymph. ACC and their class specificity were then enumerated by double fluorochrome immunofluorescence in respiratory tissues after intratracheal (i.t.) antigen **administration**. This immunization procedure produced an enhanced **IgA**-specific ACC response in the upper respiratory tract mucosa compared with either i.t. or i.p. immunization alone and this was not reflected in the regional lymph nodes. Furthermore, chronic drainage of the intestinal efferent lymphatic duct for the duration of the immunization period abrogated the enhanced response in the respiratory mucosa. These data are consistent with the concept of an intermucosal cell circuit with

respect to **IgA** cell precursors, and provide indirect evidence that **IgA** responses in the respiratory tract can be enhanced by harnessing the immune potential of GALT as a source of **IgA** precursors by appropriate immunization strategies.

L9 ANSWER 26 OF 29 MEDLINE
ACCESSION NUMBER: 84033765 MEDLINE
DOCUMENT NUMBER: 84033765 PubMed ID: 6605372
TITLE: Mucosal antibody response to **parenteral** vaccination with Haemophilus influenzae type b capsule.
AUTHOR: Pichichero M E; Insel R A
CONTRACT NUMBER: AI 07169 (NIAID)
AI 17217 (NIAID)
AI 72523 (NIAID)
SOURCE: JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1983 Nov) 72 (5 Pt 1) 481-6.
Journal code: H53; 1275002. ISSN: 0091-6749.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198312
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19831217

AB The simultaneous serum and mucosal **antibody** response to **parenteral** vaccination with the Haemophilus influenzae type b (Hib) polysaccharide capsule (PRP) was evaluated in a group of 10 children and nine adults. All subjects responded to **parenteral** vaccination with an increase in serum anticapsular **antibody**. The children's preimmunization anti-PRP **antibody** level (mean = 0.04 microgram/ml) and 3 wk postimmunization level (mean = 19.3 micrograms/ml) were lower than the adults' (preimmunization mean = 1.5 microgram/ml; postimmunization mean = 81.2 micrograms/ml). Eight of 10 children and seven of nine adults also developed a rise in **antibody** in nasal secretions. The children's mean nasal preimmunization level was 0.74 microgram/mg **IgA** and mean postimmunization level was 5.0 micrograms/mg **IgA**. The adults' mean nasal preimmunization level was 0.98 microgram/mg **IgA** and mean [illegible]immunization level was 3.0 micrograms/mg **IgA**. Salivary [illegible]esponses generally followed the pattern of nasal [illegible]es. These data suggest that [illegible]on with the Hib capsular [illegible]mucosal **antibody** response. [illegible]**ibody** responses to PRP [illegible]ts than in children, mucosal [illegible]ble.

[illegible]RIGHT 2002 ELSEVIER SCI. B.V.
[illegible]SE

[illegible]perimental study of the mode of action of [illegible]ensitization].
[illegible]PERIMENTELLE STUDIE ZUM [illegible]HANISMUS DER SPEZIFISCHEN [illegible]SIERUNG.

[illegible]er : Shears 308-4994

AUTHOR: Filipp G.; Lehmann G.; Hartung W.D.; Mootz W.
CORPORATE SOURCE: Abt. Klin. Immunol., Univ. Saarlandes, 6600 Saarbrucken, Germany
SOURCE: Allergologie, (1980) 3/3 (138-145).
CODEN: ALLRDI
COUNTRY: Germany
DOCUMENT TYPE: Journal
FILE SEGMENT: 026 Immunology, Serology and Transplantation
011 Otorhinolaryngology
LANGUAGE: German
SUMMARY LANGUAGE: English
AB During the first two stages of specific immunotherapy, we are faced with a classical booster effect. The subcutaneously **administered** allergen stimulates the immunocompetent, committed IgE plasma cells which prevail in the lamina propria. The result is a significant increase in IgE reagins. During the third phase of specific desensitization, the allergen induces the phenomenon of immunological tolerance by elimination of the specific IgE plasma cells. This results in a reduction in IgE plasma cells in the submucosa and in a corresponding decrease in specific IgE **antibodies** in the nasal secretion. The allergen after reaching the lamina propria reacts now with the predominant **IgA** plasma cells. As a result, the specific **IgA antibodies** increase. The frequently observed increase of blocking **IgG antibodies** in the blood is regarded as a result of the fact that the subcutaneously **administered** antigen during the specific desensitization passes through the subcutaneous lymph nodes and the spleen. In the spirit of this theory, the production of **IgG antibodies** is considered as an innocent, irrelevant concomitant phenomenon of the specific immunotherapy. The increase in the so-called blocking **IgG-antibodies** during the specific desensitization, many times demonstrated, is, in the sense of my working hypothesis, to be evaluated at the most as an indicator of the immunisation success. The allergenes, **injected** over years, effect an increased synthesis of all immunoglobulin classes and also of the **IgG-antibodies**. The formation of the last named **antibody** type has nothing in common with the efficiency of the immunotherapy. This discovery of mine is related to all allergic early reactions of the **mucous membranes** (exogenic-allergic rhinopathies, exogenic-allergic bronchialasthma). The situtation is different with those allergic processes which depend on the fixation of the reagins not only on the membrane of the mast cells in the submucosa but also on the membrane of the circulating basophilic leucocytes (insect sting allergies, anaphylactic shocks and shock fragments etc.) In these cases, the freely circulation **IgG-antibodies**, formed through specific densitization, are capable of neutralising immunologically the allergen which has entered the blood vessels, before reaching the reagins attached on the membrane of the basophils.

L9 ANSWER 28 OF 29 MEDLINE
ACCESSION NUMBER: 80238439 MEDLINE
DOCUMENT NUMBER: 80238439 PubMed ID: 44935
TITLE: [Comparative studies on the vaccination of mice with inactivated influenza virus **administered** by the aerosol technique, by the intranasal or

intramuscular route (author's transl)].
Vergleichende Impfung der weissen Maus mit inaktiviertem Influenza-Virus per Aerosol, intranasal und intramuskular.

AUTHOR: Neukirch M; Bauer K; Barth S

SOURCE: ZENTRALBLATT FUR BAKTERIOLOGIE, PARASITENKUNDE, INFEKTIONSKRANKHEITEN UND HYGIENE. ERSTE ABTEILUNG ORIGINALE. REIHE A: MEDIZINISCHE MIKROBIOLOGIE UND PARASITOLOGIE, (1979 Dec) 245 (4) 409-20.
Journal code: Y52; 0331570. ISSN: 0300-9688.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198009
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 19970203
Entered Medline: 19800928

AB NMRI mice were immunized intramuscular, intranasal or by Aerosol, using the ethylethylenimine inactivated and polyethylenglycolconcentrated influenza virus strain A/PR/8/34 (HO/N1). Differences in the immune response resulted from all three routes. Intranasal and intramuscular vaccination were superior to aerosol application. A possible explanation for this could be the fact that relatively small amounts of the inhaled virus antigen developed antigenic activity on the **mucous membrane**. A single vaccination by the aerosol technique gave significant protection only, if the challenge virus was applied by the same procedure. However no protection was found after intranasal challenge. Intranasal challenge on the third day post vaccination revealed that intramuscular immunization had a significant better protective effect than intranasal immunization. However from the 5th to the 10th day post vaccination this effect reversed and intranasal vaccination became superior. This immunity persisted for the whole period of observation and it was accompained by a higher titer of local **antibodies**. Similar results were obtained in experiments with aerosol challenge. Here only the intranasal vaccinated mice were completely protected after the 10th day post vaccinationem while intramuscular vaccinated animals were less protected. Sera of intramuscular immunized mice revealed a higher content in **antibodies** of the **Ig M** type and less of the **Ig G** type compared to mice vaccinated by the intranasal route.

L9 ANSWER 29 OF 29 MEDLINE

ACCESSION NUMBER: 75143348 MEDLINE
DOCUMENT NUMBER: 75143348 PubMed ID: 804792

TITLE: Techniques for eliciting mucosal immune response.

AUTHOR: Waldman R H; Ganguly R

SOURCE: ACTA ENDOCRINOLOGICA. SUPPLEMENTUM, (1975) 194 262-80. Ref: 83
Journal code: 0NF; 0370313. ISSN: 0300-9750.
PUB. COUNTRY: Denmark
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197506

ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19970203
Entered Medline: 19750619

AB Development of techniques for eliciting an immune response on mucosal surfaces is a relatively new area of clinical research. With the recognition of the existence of secretory immunity, independent of the systemic system, there was renewed interest in re-examining the conventional approach for optimal immunization techniques. A large body of data indicate that the majority of the secretory immunoglobulins and **antibody** produced to antigenic stimulation of mucosal surfaces is locally produced. Thus, **antibody** to C. albicans in the cervical or vaginal mucus has been shown to be of local origin and it predominantly belongs to the secretory **IgA** immunoglobulin class. The mechanism of antigen processing by the secretory surface leading to **antibody** formation remains a mystery, but it might be determined by the selective localization of antigens in the reticuloendothelial cells of the lamina propria, bronchi or small intestine. Usually application of antigen topically to the mucosal surface elicits local **antibody** formation to a greater extent than does **parenteral** immunization. On the other hand, a more pronounced systemic immune response is seen when the antigen is **administered** systemically. However, a number of other factors determine the quality and quantity of the immune response, e.g., the physical state of the antigen, live vs killed vaccine, dose, adjuvant, previous exposure to similar or cross-reacting antigens, and site of application of the antigen. These factors are discussed in the review. Recent observations suggest that cell mediated immunity is a component of the secretory immune system, and like the humoral mechanism, also may be partially compartmentalized.

FILE 'CAPLUS' ENTERED AT 09:43:14 ON 26 FEB 2002
L10 2363 S L2 AND ADMIN?
L11 670 S L10 AND (PARENTERAL? OR INJECT?)
L12 1 S L11 AND THIGH
L13 1 S L10 AND THIGH
L14 1 S (L12 OR L13) NOT L4

L14 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:568171 CAPLUS
DOCUMENT NUMBER: 113:168171
TITLE: Localization of Fc and Fab fragments of nonspecific polyclonal IgG at focal sites of inflammation
AUTHOR(S): Fischman, Alan J.; Rubin, Robert H.; White, Jennifer A.; Locke, Elizabeth; Wilkinson, Robert A.; Nedelman, Mark; Callahan, Ronald J.; Khaw, Ban An; Strauss, H. William
CORPORATE SOURCE: Dep. Radiol., Massachusetts Gen. Hosp., Boston, MA, 02114, USA
SOURCE: J. Nucl. Med. (1990), 31(7), 1199-1205
CODEN: JNMEAQ; ISSN: 0161-5505
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Intact IgG, Fc, Fab, and 1/2Fc (reduced and alkylated Fc) were coupled to DTPA, labeled with 111In and **administered** to rats to compare the ability of fragments of IgG to localize at focal

sites of inflammation. The following 2 sets of expts. were performed: (1) 1, 6, 24, and 48 h after **injection**, biodistribution was detd. in healthy animals; (2) localization at sites of inflammation was detd. by scintillation camera imaging of animals with deep-**thigh** infection due to Escherichia coli. The biodistribution studies demonstrated differences in kidney and liver localization: IgG < Fc < Fab < 1/2Fc (kidney), Fc < 1/2Fc < IgG < Fab (liver). The imaging studies revealed that target-to-background ratio (T/B) and percent residual activity (%RA) for IgG was greater than 1/2Fc or Fab, and T/B for IgG was greater than Fc. These studies suggest that the Fc portion of IgG is the fragment with the best imaging properties.

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 09:45:08 ON 26 FEB 2002)

L15 37 S L13
L16 29 S L10 AND FEMUR
L17 66 S (L15 OR L16) NOT L6
L18 35 DUP REM L17 (31 DUPLICATES REMOVED)
L19 15 S L18 AND (PARENTERAL? OR INJECT?)
L20 3 S L18 AND (INTRAMUSCUL? OR INTRA MUSCUL? OR QUADRICEP)
L21 16 S L19 OR L20

L21 ANSWER 1 OF 16 MEDLINE
ACCESSION NUMBER: 2001084942 MEDLINE
DOCUMENT NUMBER: 20557185 PubMed ID: 11105557
TITLE: [Human insulin-induced lipoatrophy]. Human inzulin okozta lipoatrophia.
AUTHOR: Jermendy G; Nadas J; Sapi Z
CORPORATE SOURCE: Fovarosi Bajcsy-Zsilinszky Korhaz, III. Belgyogyaszati Osztaly.
SOURCE: ORVOSI HETILAP, (2000 Oct 29) 141 (44) 2393-6. Journal code: OL8. ISSN: 0030-6002.
PUB. COUNTRY: Hungary
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Hungarian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010118

AB The medical history of a 14-year-old diabetic adolescent female patient is presented. The patient has been exclusively treated by human insulin since the manifestation of diabetes at age of 11. As a clinical curiosity lipoatrophy developed at different sites of insulin **injections** (upper arm, **thigh**, abdominal wall, buttock). The insulin **administration** technique by pen-devices was correct. The patient proved to be non-atopic without signs of insulin allergy on intracutan tests. On histological examination, "lipoblastoma-like" alterations without signs of local immune mechanisms and no inflammatory cell infiltrates were found at the site of lipoatrophy. The histological findings suggested dedifferentiation of adipose tissue mediated probably by elevated local tumor necrosis factor-alpha. Immunological consequences of previous human insulin treatment were documented by high insulin-specific **IgG** and IgE **antibody** titer, however, no clinical signs of immunogenic insulin resistance were found. Switching to insulin analogue (insulin lispro) before main

meals no further lipoatrophic areas were observed despite of using human NPH-insulin for basal insulin supplementation. Insulin analogue (insulin lispro) may be useful for treating diabetic patients with lipoatrophy secondary to previous human insulin treatment.

L21 ANSWER 2 OF 16 MEDLINE
ACCESSION NUMBER: 2000465465 MEDLINE
DOCUMENT NUMBER: 20471375 PubMed ID: 11021392
TITLE: Antibacterial properties of Pseudomonas aeruginosa immunotype 1 lipopolysaccharide-specific monoclonal antibody (MAb) in a murine **thigh** infection model: combined effects of MAb and ceftazidime.
AUTHOR: Akiyama M; Oishi K; Tao M; Matsumoto K; Pollack M
CORPORATE SOURCE: Department of Internal Medicine, Institute of Tropical Medicine, Nagasaki University, Japan.
SOURCE: MICROBIOLOGY AND IMMUNOLOGY, (2000) 44 (8) 629-35. Journal code: MX7. ISSN: 0385-5600.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010208

AB A murine monoclonal **antibody** (MAb) specific for the Pseudomonas aeruginosa immunotype 1 (It-1) lipopolysaccharide (LPS) O-side chain was evaluated in terms of its in vitro bactericidal opsonophagocytic activity and in vivo bacterial killing in a mouse **thigh** infection model. An immunoglobulin (Ig) G2a MAb Ld3-2F2, specific for It-1 LPS, mediated in vitro complement-dependent opsonophagocytic killing at a concentration of 10 microg/ml. MAb-mediated, complement-dependent killing also occurred in the absence of neutrophils at serum concentrations in excess of 20%. A remarkable synergy was observed in opsonophagocytic assays between MAb Ld3-2F2 (0.5 microg/ml) and ceftazidime (1/4 MIC). The **administration** of MAb Ld3-2F2 at a level of 1 microg resulted in a significant decrease in the number of bacteria in the **thigh** muscles of normal mice, while 100 microg of the same MAb was required for one log of reduction in the number of bacteria at the same site in neutropenic mice. The combined therapy with MAb Ld3-2F2 and ceftazidime provided a significant reduction in the density of bacteria in the **thigh** muscle at 9 hr post-infection in normal and neutropenic mice as compared with those after treatment alone or with no treatment ($P < 0.01$). These favorable in vitro and in vivo interactions of an LPS-specific **IgG** MAb and ceftazidime strongly support their potential for use in therapy, combined with an LPS-reactive MAb and **parenteral** antipseudomonas beta-lactam antibiotics in the therapy of systemic Pseudomonas infections in normal and neutropenic hosts.

L21 ANSWER 3 OF 16 MEDLINE
ACCESSION NUMBER: 2000186795 MEDLINE
DOCUMENT NUMBER: 20186795 PubMed ID: 10724200
TITLE: Intralesional therapy with anti-CD20 monoclonal **antibody** rituximab in primary cutaneous

B-cell lymphoma.

AUTHOR: Heinzerling L; Dummer R; Kempf W; Schmid M H; Burg G
CORPORATE SOURCE: Department of Dermatology, University Hospital Zurich, Switzerland.
SOURCE: ARCHIVES OF DERMATOLOGY, (2000 Mar) 136 (3) 374-8. Journal code: 6WU; 0372433. ISSN: 0003-987X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000407
Last Updated on STN: 20000407
Entered Medline: 20000330

AB BACKGROUND: We report the use of a new treatment modality in 2 patients with primary cutaneous **B-cell** lymphoma.
In a 58-year-old woman with progressive nodular lesions on the scalp and face, several treatment attempts either failed or could not be used because of severe adverse effects and underlying epilepsy. The patient declined radiotherapy. A 30-year-old man presented with recurrence of tumor nodules occipitally, thoracically, on the arm, and on the right **thigh** after several excisions.
OBSERVATIONS: Intralesional **injection** of rituximab, a chimeric **antibody** directed against the CD20 transmembrane antigen present in malignant and normal **B cells**, resulted in partial regression of tumor nodules. No adverse effects occurred except pain during or shortly after **injection** and, in one patient, a slight rise in body temperature. Due to the treatment a prolonged complete disappearance of **B cells** from peripheral blood samples was observed.
CONCLUSION: Intralesional rituximab therapy is a nontoxic and effective treatment for cutaneous **B-cell** lymphoma that deserves further investigation in larger clinical trials.

L21 ANSWER 4 OF 16 MEDLINE
ACCESSION NUMBER: 97196940 MEDLINE
DOCUMENT NUMBER: 97196940 PubMed ID: 9044029
TITLE: Evaluation of hypersensitivity to microencapsulated ampicillin in guinea pigs.
AUTHOR: Barsoum I S; Kopydlowski K M; Cuenin P; Setterstrom J A
CORPORATE SOURCE: US Army Dental Research Detachment, Walter Reed Army Institute of Research, Washington, DC 20307-5300, USA.
SOURCE: JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY, (1997 Jan) 39 (1) 63-9.
Journal code: HD7; 7513617. ISSN: 0305-7453.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970523
Last Updated on STN: 19970523
Entered Medline: 19970515

AB The purpose of this study was to determine if the sustained release of ampicillin from a biodegradable drug-delivery system

(microencapsulated ampicillin anhydrate (MEAA)) will increase or decrease the intensity of a hypersensitivity reaction compared with that observed with free drug. Ovalbumin, which is known to elicit a marked hypersensitivity reaction in guinea pigs, and microencapsulated ovalbumin (MOVA) were tested in parallel with ampicillin and MEAA. Guinea pigs were sensitized biweekly by subcutaneous and **intramuscular injections** of ampicillin, MEAA, ovalbumin, MOVA or placebo microspheres (test articles), each mixed with Freund's adjuvant, and challenged 2 weeks later, intradermally, with the free compounds. In a separate set of experiments, guinea pigs were sensitized by implantation of the same agents in the caudal **thigh** of anaesthetized animals. Skin allergic reactions were tested at 1 and 3 weeks following local implantation of the test articles. Sera of sensitized guinea pigs were tested for specific **IgG antibodies** by enzyme-linked immunosorbent assay, and skin samples from the site of the inflammatory reaction were fixed, stained and evaluated histologically. Guinea pigs sensitized systemically with MEAA or MOVA showed smaller, but not statistically different skin allergic response than animals given corresponding free compounds. However, guinea pigs sensitized by local implantation of MEAA showed a significantly lower inflammatory response ($P < 0.0001$) than those given an equivalent dose of the free drug. Guinea pigs sensitized with placebo microspheres showed a low inflammatory skin reaction which was similar to those sensitized with all doses of MEAA. There was no significant difference in specific **IgG antibody** response in the sera of guinea pigs sensitized locally with either free or microencapsulated ampicillin or ovalbumin. Histology of skin revealed a milder inflammatory reaction with MEAA or MOVA than with ampicillin or ovalbumin, respectively. We conclude that the encapsulated ampicillin or ovalbumin and subsequent release of each agent will elicit a reduced hypersensitivity reaction in guinea pigs than will the free agent.

L21 ANSWER 5 OF 16 MEDLINE
ACCESSION NUMBER: 96360140 MEDLINE
DOCUMENT NUMBER: 96360140 PubMed ID: 8719108
TITLE: The bone marrow as a site of antibody production after a mucosal immunization.
AUTHOR: Benedetti R; Massouh E; Flo J
CORPORATE SOURCE: Department of Biological Chemistry, Faculty of Exact and Natural Sciences, University of Buenos Aires, Argentina.
SOURCE: IMMUNOLOGY LETTERS, (1995 Dec) 48 (2) 109-15. Journal code: GIH; 7910006. ISSN: 0165-2478.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19961008
Last Updated on STN: 19961008
Entered Medline: 19960923

AB To study the importance of the bone marrow in the production of specific **antibodies** after a mucosal immunization with cholera toxin, the **IgG**, **IgA** and **IgM** specific **antibody** forming cells were evaluated by ELISPOT in Peyer patches, mesenteric lymph node (MLN), spleen, blood and

bone marrow (BM). When 50-day-old rats were immunized intra-Peyer patches, a similar number of **IgG** and **IgA** antitoxin **antibody** forming cells (AFC) were found in the BM, whereas in the other lymphoid tissues a higher number of **IgG** antitoxin AFC were found. In all sites the peak of AFC was obtained 2 weeks after immunization. The **administration** of CT to 35-week-old rats resulted in a stronger immune response in all lymphoid tissues studied, but the proportion of antitoxin AFC contributed by the BM had not changed. One oral dose of cholera toxin resulted in a low number of antitoxin AFC, whereas when two or three doses of CT were **administered** orally an increase in the number of AFC was observed in the BM, reaching similar or higher numbers of **IgG** and **IgA** AFC than in the spleen. In all cases the highest number of AFC/10(6) cells was observed in the MLN, whereas antitoxin AFC were not found in the blood. The total number of AFC recovered from each organ was calculated taken into account that the BM of one **femur** represents 9% of the total BM. So, it was found that the BM is an important site in the production of **IgG** antitoxin **antibodies**, being the main site in the **IgA** antitoxin **antibody** production.

L21 ANSWER 6 OF 16 MEDLINE
ACCESSION NUMBER: 96335196 MEDLINE
DOCUMENT NUMBER: 96335196 PubMed ID: 8706051
TITLE: 99mTc-CD19 monoclonal **antibody** is not useful for imaging of **B cell** non-Hodgkin's lymphoma.
AUTHOR: Vervoordeldonk S F; Heikens J; Goedemans W T; Merle P A; von dem Borne A E; van Royen E A; Slaper-Cortenbach I C; van Oers R H
CORPORATE SOURCE: Central Laboratory, Red Cross Blood Transfusion Service, University of Amsterdam, The Netherlands.
SOURCE: CANCER IMMUNOLOGY, IMMUNOTHERAPY, (1996 Jun) 42 (5) 291-6.
Journal code: CN3; 8605732. ISSN: 0340-7004.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19960919
Last Updated on STN: 19970203
Entered Medline: 19960910

AB In this study we investigated the applicability of 99mTc-labeled CD19 monoclonal **antibody** (mAb) for tumor imaging in patients with **B cell** non-Hodgkin's lymphoma. A 1-mg sample of murine CD19 mAb was labeled with approximately 550 MBq [99mTc]pertechnetate. The labeled mAb was **administered** i.v. to seven patients, four without and three with pretreatment with 10 mg unlabeled CD19 mAb. The number of circulating **B cells** was decreased by 44 +/- 5% 1 h after **injection** of the radiolabeled mAb. Peripheral **B cells** were coated with CD19, resulting in partial modulation of CD19, most pronounced in the three pretreated patients. Whole-body images were obtained with a gamma camera and compared with results obtained by conventional imaging techniques. Initially, blood-pool activity dominated, whereas 24 h after **injection** the radioactivity

was mainly located in the spleen, kidneys and liver. In two patients, a lesion in the spleen appeared as an unlabeled spot. In one patient, a lesion in the **femur**, which was detected by computed tomography (CT) and gallium-67 scans, was also seen on the CD19 scan from 1 h after **administration** of the radioimmunoconjugate onwards. Good imaging of bone marrow infiltration was observed in one of three patients. Lymph node involvement was not observed in any of the patients in whom affected lymph nodes were detected by CT or gallium-67 scan. In conclusion, in the present study radioimmunodetection with 99mTc-labeled CD19 mAb was found to be inferior to CT and gallium-67 scanning in the diagnosis of patients with **B cell** non-Hodgkin's lymphoma.

L21 ANSWER 7 OF 16 MEDLINE
ACCESSION NUMBER: 90170197 MEDLINE
DOCUMENT NUMBER: 90170197 PubMed ID: 2307538
TITLE: Disseminated or localized growth of a human B-cell tumor (Daudi) in SCID mice.
AUTHOR: Ghetie M A; Richardson J; Tucker T; Jones D; Uhr J W; Vitetta E S
CORPORATE SOURCE: Department of Microbiology, University of Texas Southwestern Medical Center, Dallas 75235.
SOURCE: INTERNATIONAL JOURNAL OF CANCER, (1990 Mar 15) 45 (3) 481-5.
Journal code: GQU; 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199004
ENTRY DATE: Entered STN: 19900601
Last Updated on STN: 19980206
Entered Medline: 19900410

AB A human Burkitt lymphoma (Daudi) has been grown in the mutant mouse called C.B-17 SCID. Twenty-eight days after s.c. **injection** of Daudi cells, a palpable tumor grew only at the site of **injection** in all **injected** mice. In contrast, after intravenous (i.v.) or intraperitoneal (i.p.) **injection**, macroscopic, disseminated tumors developed. Following i.v. inoculation, tumors grew in the lungs, kidneys, ovaries and adipose tissue, and microscopic tumor infiltrates were observed in the spleen, bone marrow, spinal column and **femur**, whereas after i.p. **injection**, the tumors were localized in the abdomen, liver, spleen, ovaries and muscular tunics of the gut, but did not disseminate into the lung or bone marrow. The growth pattern and phenotype of the Daudi cells were similar whether the inoculated tumor cells were derived from the in vitro cell line or from in vivo passaged tumors. The survival time of the tumor-bearing animals was dependent on the dose of i.v.-**administered** Daudi cells; as few as 100 cells caused death. All mice **injected** i.v. showed paresis or paralysis of the hind legs just prior to death. This was associated with the presence of neoplastic nodules within the spinal canal. Two surface antigens on Daudi cells (CD19 and CD22) were stably expressed in all the neoplastic lesions. Radiolabelled anti-CD22 **antibodies** localized in organs infiltrated with tumor, but did not penetrate primary s.c. tumors. This model of disseminated vs. solid tumor should prove useful for

evaluating the efficacy of different types and doses of therapeutic **antibodies**, immunoconjugates and immunotoxins prepared from anti-human **B-cell antibodies**.

L21 ANSWER 8 OF 16 MEDLINE
ACCESSION NUMBER: 89275615 MEDLINE
DOCUMENT NUMBER: 89275615 PubMed ID: 3150699
TITLE: Effect of intravenous immunoglobulin on a spontaneous inhibitor to factor VIII.
AUTHOR: Newland A C; Macey M G; Moffat E H; Ainsworth M; Colvin B T
CORPORATE SOURCE: Department of Haematology, London Hospital, Whitechapel.
SOURCE: CLINICAL AND LABORATORY HAEMATOLOGY, (1988) 10 (4) 435-42.
Journal code: DKF; 7907061. ISSN: 0141-9854.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198907
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19890717

AB A 71-year-old woman with a spontaneous anti-factor VIII inhibitor fractured her right wrist and 2 months later her left **femur** . She received treatment with porcine factor VIII for the first fracture and developed a secondary anti-porcine **antibody** response (from 10 to 200 Bethesda units). Following the second fracture she received intravenous immunoglobulin (i.v. **IgG**) (0.4 g/kg day for 5 days) in an attempt to reduce **antibody** activity. Despite further treatment with porcine factor VIII, the **antibody** level declined instead of rising as expected and the anti-human **antibody** activity also declined. We were not able to demonstrate neutralizing activity to her **antibody** but did demonstrate a reduced helper: suppressor ratio and reduced **B-cell** numbers and function after treatment with i.v. **IgG**. These changes were transient and as **B-cell** function improved over the following 4 months, her anti-human activity returned toward its previous level. Anti-porcine activity remained at its previous low level. We speculate that one of the mechanisms of action of i.v. **IgG** may be a direct cellular effect influencing both T-suppressor and **B-lymphocyte** function.

L21 ANSWER 9 OF 16 MEDLINE
ACCESSION NUMBER: 85197689 MEDLINE
DOCUMENT NUMBER: 85197689 PubMed ID: 3994308
TITLE: Radioimmunodetection of gliomas by **administration** of radiolabelled monoclonal antibodies. Experimental data.
AUTHOR: Stavrou D; Mellert W; Bilzer T; Senekowitsch R; Keiditsch E; Mehraein P
SOURCE: ANTICANCER RESEARCH, (1985 Mar-Apr) 5 (2) 147-56.
Journal code: 59L; 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 198505
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19850528

AB Radiolabelled monoclonal **antibodies** (McAbs) raised against membrane components of an experimental rat glioma (79FR-G-41) were **administered parenterally** to immunodeficient mice bearing glioma grafts for tumor radioimmunodetection by external imaging. Purified McAbs (14AC1) of IgG2a isotype were labelled with Na131I (2mCi/50ml) using the Chloramin-T method. As control, for non-specific uptake of proteins in the tumor, normal mouse **IgG** were also iodinated. For radioimaging, nude mice bearing gliomas in the **thigh** muscle were **injected** intravenously with 15 micrograms of the 131I-McAb with an activity of approximately 150 mu Ci. Control tumor-bearing animals received the same amount of mouse 131I-**IgG**. Scans obtained immediately after **injecting** the intact 131I-14AC1 **antibody** and at 24, 48, 72, and 96 hours demonstrated accumulation in the tumor. The tumor was clearly visible 48 hours following **injection** of 131I-labelled **antibody**. At 96 hours after **injection**, the McAb showed a clearly higher uptake into the tumor as the control **IgG**. The biodistribution of the **injected antibody** was studied at 96 hours after **injection** following the last gamma-imaging. At this time the blood activity was still high, but the maximum activity was found in the tumor for the specific McAb. Using the 131I-14AC1 to image glioma transplants, it could be shown that grafts are permeable for the McAb. The time-course experiments **administering** 131I-14AC1 **antibody** and normal mouse 131I-**IgG**, demonstrated that the localization of 131I-I4AC1 **antibody** in glioma grafts is the result of specific antigen binding. The scintigrams using intact **antibody** without background subtraction provided adequate tumor visualization, but the activity in the blood was high even 96 hours after **injection**. More rapid clearance of blood - pool radioactivity would possibly be achieved with F(ab')2 fragments. These in vivo glioma imaging studies, together with related in vitro binding tests, indicate the potential value of monoclonal antiglioma **antibodies** not only for clinical tumor radioimmunodetection, but also for the evaluation of immunotherapeutic approaches to the glioma disease of man.

L21 ANSWER 10 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:480943 BIOSIS
DOCUMENT NUMBER: PREV199800480943
TITLE: Unusual presentation of cutaneous vasculitis.
AUTHOR(S): Hafeez, Zeba Hasan (1)
CORPORATE SOURCE: (1) 27A Khayaban-1-Tanzeem, Defence Housing Society, Phase 5, Karachi Pakistan
SOURCE: International Journal of Dermatology, (Sept., 1998) Vol. 37, No. 9, pp. 687-690. ISSN: 0011-9059.
DOCUMENT TYPE: Article
LANGUAGE: English

AB A 12-year-old boy from a village near Sukkur presented to the Civil Hospital, Karachi, Pakistan, in January 1992, with widespread black discoloration and ulcers of the lower extremities and focal areas of

involvement of the upper extremities and face. The patient was previously healthy, when he suddenly developed low grade fever and severe pain on the left side of the chest for which he was given two unknown white tablets. His fever gradually became high, and next morning he was unable to walk and had erythematous patches on his lower extremities, nose, and posterolateral aspects of the upper extremities. He also developed watery diarrhea without blood or mucus and was incontinent. He was treated with a single dose of cotrimoxazole, furazolidone, and mefenamic acid. Oral rehydration salts were also given. His diarrhea improved, but the erythematous patches started to become black. Other symptoms included frequency and difficulty in passing urine, with only a few drops passed each time. He was hospitalized in Sukkur where oral antimicrobials (erythromycin, clindamycin) and **parenteral** steroids (dexamethasone, 4 mg, six hourly) were **administered**. The latter was gradually tapered over 15 days. The urinary symptoms improved after 1 day of hospitalization and treatment. Focal areas of the affected skin of the ears, face, and upper extremities became dry and sloughed off. The lesions were tender. There was no past history of sore throat, jaundice, joint pains, or blood transfusion. He had an episode of left-sided chest pain 1 year ago for which he was given medication. Five years ago he had a traumatic fracture of the lower leg. On examination, patchy but extensive black discoloration of the feet, lower legs, knees, and posterolateral aspects of the **thighs** was seen. Large ulcers were present on the buttocks and upper extremities. Ulcers were also seen on the nose, cheeks, lateral aspects of the pinna, upper arms, and elbows (Figs 1 and 2). His temperature was 98.6 degreeF orally, pulse rate was 90/min (regular), respiratory rate was 20/min, and blood pressure was 90/50 mmHg. The patient was non-toxic, with no apparent systemic involvement on clinical examination. In the initial investigations, hemoglobin was 11 g%, erythrocyte sedimentation rate (ESR) was 47 mm (first hour), and leukocytosis was 36,250/mm3 reverting to normal on clinical improvement. The ESR after rising to 56 mm (first hour) decreased to 15 mm (first hour) with control of the infection. Total serum proteins were 5.1 g/dL with albumin 2.5 g/ dL. Pus oozing from the ulcers revealed Pseudomonas aeruginosa and Staphylococcus aureus (coagulass positive) on culture. The anti-streptolysin (ASO) titer was between 100 and 333 Todd units. C3 was 1.11 g/dL (N 0.7-1.80) and C4 0.64 g/dL (N 1.15-0.7). Studies with normal or negative results included several urinalyses, blood cultures, liver function tests, blood urea nitrogen, serum creatinine, antinuclear **antibodies** (ANA), anti smooth muscle **antibodies**, anti mitochondrial **antibodies** , anti double-stranded DNA **antibodies**, cryoglobulins, hepatitis B surface antigen, Coombs test, and chest X-ray. Gram stains of skin sections were negative for any organisms. Skin biopsy showed ulceration and pustules in the epidermis, with the underlying dermis having multiple areas of severe vasculitis with fibrinoid necrosis in the vessel walls and neutrophil polymorph infiltration. Small- and medium-sized vessels were involved, with no evidence of granuloma. Direct immunofluorescence showed **immunoglobulin M** (IgM) (focal) and IgG in the vessel walls and at the dermo-epidermal junction and C3 (++) at the dermoepidermal junction. **IgA** and fibrin were negative. The patient was given prednisolone, 35 mg orally daily, which was gradually reduced to 20 mg daily. At this dose, new vesicles appeared on the healing skin of the lower legs, but disappeared when

the steroid was increased to 35 mg again. Antimicrobials (aminoglycosides, cephalosporins, penicillins, and monobactams) were **administered** according to microbial culture and sensitivity results for the cutaneous infection with Pseudomonas aeruginosa and Staphylococcus aureus. Healing occurred with autoamputation of several digits of the feet. The patient was discharged on azathioprine, 25 mg, and prednisolone, 25 mg, daily. The latter was reduced by 2.5 mg per week to 10 mg (after 6 weeks) on alternate days. It was noted that, on reduction of immunosuppressives, vesicles typically appeared around the ankles. Immunosuppressives were tapered off and completely stopped after 2 years (March 1994). The patient was examined again in February 1997 (Figs 3 and 4). There was complete remission (for 3 years).

L21 ANSWER 11 OF 16 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97310648 EMBASE
DOCUMENT NUMBER: 1997310648
TITLE: Detection of experimental infections with (99m)Tc-labeled monoclonal antibodies against TNF-.alpha. and interleukin-8.
AUTHOR: Welling M.; Feitsma H.I.J.; Calame W.; Pauwels E.K.J.
CORPORATE SOURCE: Dr. E.K.J. Pauwels, Department of Radiology, Division of Nuclear Medicine, Leiden University Medical Centre, P.O. Box 9600, NL-2300 RC Leiden, Netherlands
SOURCE: Nuclear Medicine and Biology, (1997) 24/7 (649-655). Refs: 48
ISSN: 0969-8051 CODEN: NMBIEO
PUBLISHER IDENT.: S 0969-8051(97)00118-2
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 023 Nuclear Medicine
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB This study was designed to assess monoclonal **antibodies** (MAbs) directed against tumor necrosis factor-.alpha. (TNF-.alpha.) (anti-TNF) or interleukin-8 (anti- IL-8) as radioactive agents for the detection of Staphylococcus aureus- or Klebsiella pneumoniae-infected **thighs** in mice. At 5 min (acute infection) or 20 h (established) post-infection, 20 .mu.g of the (99m)Tc-labeled MAbs were **injected**. At various time intervals, the accumulation of the radiotracer in the infected **thighs** was assessed and expressed as a target-to-nontarget (T/NT) ratio. The binding of (99m)Tc-labeled MAbs to circulating mononuclear cells and granulocytes was quantitated 20 h after **injection**. The pharmacokinetics of the MAbs, in relation to the control agents (99m)Tc- labeled polyclonal human immunoglobulin (IgG) and a (99m)Tc-labeled nonspecific IgG1 MAb, were also studied. In acute infections, (99m)Tc-anti- TNF accumulated to a higher extent ($p < 0.05$) in S. aureus-infected **thighs** in mice until 4 h after the **injection** than (99m)Tc-IgG and was higher at 0.25 h in K. pneumoniae-infected mice ($p < 0.03$) compared with (99m)Tc-IgG. In established S. aureus and K. pneumoniae infections, (99m)Tc-anti-IL-8 detected the infection more intensely than (99m)Tc-IgG until 1 h after **injection**. In both S. aureus and K. pneumoniae infections,

localization of sites of infection correlates ($p < 0.05$) with increased binding of the (99m)Tc-labeled MAbs to granulocytes and mononuclear cells in both acute and established infections. It was concluded that (99m)Tc-labeled MAbs, directed against TNF-.alpha. and IL-8, accumulate in bacterial infections in mice to a higher extent than does (99m)Tc-**IgG** after infection and is related to the binding of the **antibodies** to blood leukocytes. With these (99m)Tc-labeled MAbs, information might be gained about the development of an infection.

L21 ANSWER 12 OF 16 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94051237 EMBASE
DOCUMENT NUMBER: 1994051237
TITLE: Use of bremsstrahlung radiation to monitor Y-90 tumor and whole body activities during experimental radioimmunotherapy in mice.
AUTHOR: Dillehay L.E.; Mayer R.; Zhang Y.G.; Song S.-Y.; Shao Y.; Mackensen D.G.; Williams J.R.
CORPORATE SOURCE: Radiobiology Laboratory, Johns Hopkins Oncology Center, 600 North Wolfe Street,Baltimore, MD 21287-5001, United States
SOURCE: Cancer, (1994) 73/SUPPL. (945-950).
ISSN: 0008-543X CODEN: CANCAR
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 016 Cancer
023 Nuclear Medicine
037 Drug Literature Index
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background. Large differences in uptake between tumors, even for the same size, frequently observed in clinical and experimental radioimmunotherapy (RAIT), make monitoring of uptake in individual tumors imperative in comparing protocols. 90Y, widely-used for RAIT, emits no gamma radiation and absorption of the beta particle in tissue makes its detection unsuitable for in vivo monitoring. We tested whether bremsstrahlung radiation, produced when betas are decelerated by nuclei, could be used to monitor tumor uptake. Methods. Subcutaneous human LS174T colon carcinoma tumors were grown in the upper **thigh** of nude mice and labeled antibody **injected** intracardially. With the tumor placed in the 2 cm-diameter aperture in a lead collimator, photons with energies from 100 to 200 keV transmitted through plastic, which absorbed the beta particles, were counted to maximize shielding from the rest of the body. The contribution of the normal tissues was subtracted by counting the non-tumor-bearing leg in the same position. Excretion was calculated from whole body activity determined by removing the collimator, placing the mouse in a syringe surrounded by tissue-equivalent material 10 cm from the detector, and counting photons between 200 and 740 keV to minimize the effect of tissue attenuation. Results. For tumors larger than 0.14 gm, a good correlation was obtained between the in vivo bremsstrahlung measurements and the measurements on excised tumors in a calibrated well counter. Similar excretion rates observed in all the animals suggested that the whole body counting was accurate. Conclusions. Bremsstrahlung detection appears feasible and reliable for monitoring both tumor and whole body activities.

L21 ANSWER 13 OF 16 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 91223610 EMBASE
DOCUMENT NUMBER: 1991223610
TITLE: Comparison of 99Tcm-labelled monoclonal anti-granulocyte **antibody** and 111In-labelled **IgG** for the detection of focal sites of infection in rats.
AUTHOR: Juweid M.; Fischman A.J.; Rubin R.H.; Baum R.; Strauss H.W.
CORPORATE SOURCE: Division of Nuclear Medicine, Massachusetts General Hospital, 55 Fruit Street, Boston, MA 02114, United States
SOURCE: Nuclear Medicine Communications, (1991) 12/7 (637-644).
ISSN: 0143-3636 CODEN: NMCODC
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
023 Nuclear Medicine
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The abilities of 99Tcm-labelled monoclonal anti-human granulocyte **antibody** (AGAb) and 111In-labelled nonspecific polyclonal human immunoglobulin (**IgG**) to localize at focal sites of inflammation were compared in rats with deep **thigh** infection due to E. coli. The radiolabelled **antibodies** were coadministered followed 4-6 and 24 h later by imaging and biodistribution studies. At 4-6 h after **injection**, the target to background ratio (T/B, lesion to contralateral leg) and percentage residual activity (% RA, counts in the lesion/total body counts) were nearly identical for both **antibody** preparations. At 24 h, T/B and % RA increased significantly ($P<0.001$) for both proteins but differences between the agents were not significant. In vitro analysis of the binding of AGAb and human polyclonal **IgG** to rat granulocytes showed a low level of binding with both agents. These results suggest that the primary mechanism of localization, by either **antibody** preparation in this model, is not antigen related. 111In -labelled nonspecific human **IgG** and 99Tcm-AGAb are equivalent reagents for the detection of focal sites of infection in the rat.

L21 ANSWER 14 OF 16 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 87043962 EMBASE
DOCUMENT NUMBER: 1987043962
TITLE: Effects of physical exercise on insulin absorption in insulin-dependent diabetics. A comparison between human and porcine insulin.
AUTHOR: Fernqvist E.; Linde B.; Ostman J.; Gunnarson R.
CORPORATE SOURCE: Department of Medicine, Huddinge Hospital, S-141 86 Huddinge, Sweden
SOURCE: Clinical Physiology, (1986) 6/6 (489-498).
CODEN: CLPHDU
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
003 Endocrinology

019 Rehabilitation and Physical Medicine
LANGUAGE: English
AB Nine insulin-dependent diabetics with undetectable plasma C-peptide (<0.05 nmol l-1) and without insulin **antibodies** (insulin binding to **IgG**<0.05 Ul-1) received subcutaneous **injections** of 10 U 125I-labelled soluble human or porcine insulin in the **thigh** on 2 consecutive days. Disappearance rates of 125I were monitored continuously by external counting and plasma insulin levels were determined during rest for 30 min, bicycle exercise of moderate intensity for 40 min, and 60 min recovery. Subcutaneous blood flow was measured concomitantly in the contralateral **thigh** by the 133Xenon clearance technique. During the initial period of rest human insulin was absorbed approximately 40% faster than its porcine analogue (first order rate constants 0.37.+-.0.06 vs 0.27.+-.0.06% min-1, P<0.05) and the increment of the area under the plasma insulin curve was greater after human than after porcine insulin (184.+-.46 vs 112.+-.42 mUl-1 min, P<0.05). Exercise enhanced the absorption rates for both 125I-insulins to 0.50.+-.0.06 and 0.48.+-.0.10% min-1 for human and porcine insulin, respectively (P<0.05). This increase was less pronounced for human compared to porcine insulin (49.+-.19 vs 105.+-.40%, P=0.06). During exercise plasma insulin rose to 37.+-.5 mUl-1 after human and 30.+-.5 mUl-1 after porcine insulin and the areas under the plasma insulin curves were similar. During the recovery phase the absorption rates decreased slightly compared to the exercise value for both insulins. The blood glucose lowering effect was similar for the two insulins. Subcutaneous blood flow was not significantly altered by exercise in either group. It is concluded that during rest human soluble insulin is more rapidly absorbed than porcine insulin. Physical exercise tends to increase porcine insulin absorption more and eliminates the basal difference in the absorption kinetics between human and porcine insulin. The increased insulin absorption during exercise is not coupled to corresponding changes in the subcutaneous blood flow.

L21 ANSWER 15 OF 16 JICST-EPlus COPYRIGHT 2002 JST
ACCESSION NUMBER: 960722590 JICST-EPlus
TITLE: One-month Subcutaneous Toxicity Study of Recombinant Human Basic Fibroblast Growth Factor(KCB-1) in Rats with and without One-month Recovery Study.
AUTHOR: NAKAMURA TOSHIYUKI; SUGIMOTO HAJIME; NAKAMURA MARIKO; SHIBANUSHI TOSHIYUKI; MARUYAMA KIYOSHI; ITO AKIRA; IKAI MASANORI; HASHIMOTO KAZUTO; KUDO MINAO
CORPORATE SOURCE: Kakenseiyaku Kaiken
SOURCE: Iyakuhin Kenkyu, (1996) vol. 27, no. 7, pp. 379-408. Journal Code: F0456B (Fig. 6, Tbl. 25, Ref. 7) CODEN: IYKEDH; ISSN: 0287-0894
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New
AB A 1-month subcutaneous toxicity study followed by a 1-month recovery study of recombinant human basic fibroblast growth factor(KCB-1) was performed using Crj:CD(SD) rats at doses of 40, 200 and 1000.MU.g/kg/day to estimate the no-observed-adverse-effect level(NOAEL). 1. As regards general condition, thickening and soft nodule formation at the **injection** sites were noted in the 100.MU.g/kg group. One male animal of the 1000.MU.g/kg group died

accidentally on day 7 of the dosing period. 2. Slight suppressions of body weight gain and food intake were observed in males of the 1000.MU.g/kg group. 3. Anemia was seen in the 1000.MU.g/kg group during the dosing period. The **IgG** and **IgM** **antibody** titers were elevated in all dosing groups. 4. Significant decreases in albumin and A/G were observed in the 1000.MU.g/kg group at the end of dosing and during the recovery period. 5. In urinalysis, some increase in protein excretion was seen in the 1000.MU.g/kg group in the dosing and recovery periods though it was not statistically significant. 6. At autopsy, congestion and hemorrhage, soft nodules, edema and hard nodules at the **injection** site were observed in the dosing groups. Splenomegaly was additionally seen in males of the 200 and 1000.MU.g/kg groups. 7. Significant increases in the absolute and relative weights of spleen and liver were noted in the 200 and 1000.MU.g/kg groups during the dosing and recovery periods and in kidneys and ovaries of females of the 1000.MU.g/kg group during the recovery period. 8. In histopathology, an increase of trabecular bone was seen in bone marrows of **femur** and sternum in the 1000.MU.g/kg group. In spleen, congestion and increase of the erythroblast series were observed in the 200 and 1000.MU.g/kg groups. In liver, increase of the erythroblast series was observed in the 200 and 1000.MU.g/kg groups. (author abst.)

L21 ANSWER 16 OF 16 JICST-EPlus COPYRIGHT 2002 JST
ACCESSION NUMBER: 940090604 JICST-EPlus
TITLE: A Case of Hoffmann Syndrome with Blocking Type TSH Receptor Antibody.
AUTHOR: KOMINE SATOSHI; SAITO KAYOKO; YOSHIDA MAKOTO; MATSUZAKI MIHOKO; SUZUKI HARUKO; SHISHIKURA KEIKO; FUKUYAMA YUKIO
SATO KANJI; TSUSHIMA TOSHIO
CORPORATE SOURCE: Tokyo Women's Medical College
Tokyo Women's Medical College, School of Medicine, Inst. of Clinical Endocrinology
SOURCE: Tokyo Joshi Ika Daigaku Zasshi (Journal of Tokyo Women's Medical College), (1993) vol. 63, pp. E322-E330. Journal Code: G0684A (Fig. 9, Tbl. 3, Ref. 24)
CODEN: TJIZAF; ISSN: 0040-9022
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New
AB We report herein a 16 year old patient suffering from TRAb(TSH receptor **antibody**) positive hypothyrodism which induced Hoffmann syndrome. By using a highly-sensitive bioassay for TSH, which measures 125I incorporation and denovosynthesized 125I-T4 secretion into the culture medium, the patient's **IgG** with TRAb was demonstrated to be the TSH-stimulation-blocking **antibody**. The **administration** of thyradin-S normalized his symptoms and thyroid functions, but mounding phenomenon improved slowly. The pathological findings on a muscle needle biopsy of the right **quadriceps** femoris muscle included type I fiber predominance by myosin-ATPase staining, which was confirmed by a differential histogram of muscle fibers. (author abst.)

FILE 'CAPLUS' ENTERED AT 09:55:32 ON 26 FEB 2002
L22 3 S L10 AND FEMUR
L23 3 S L22 NOT (L4 OR L14)

L23 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:599544 CAPLUS
DOCUMENT NUMBER: 125:269375
TITLE: Intraperitoneal indium-111- and yttrium-90-labeled human IgM (AC6C3-2B12) in nude mice bearing peritoneal carcinomatosis
AUTHOR(S): Quadri, Syed M.; Malik, Atif B.; Chu, Hung B.; Freedman, Ralph S.; Vriesendorp, Huibert M.
CORPORATE SOURCE: M.D. Anderson Cancer Center, University Texas, Houston, TX, 77030, USA
SOURCE: J. Nucl. Med. (1996), 37(9), 1545-1551
CODEN: JNMEAQ; ISSN: 0161-5505
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Radiolabeled monoclonal antibodies are utilized increasingly for the diagnosis and treatment of human cancer. Tumor targeting of radiolabeled human monoclonal IgM improves with compartmental **administration** and might be useful for the diagnosis or treatment of peritoneal carcinomatosis. A human monoclonal **antibody IgM**.lambda. (AC6C3-B12) reactive with human adenocarcinomas was conjugated to isothiocyanato-2-benzyl-3-methyl-diethylenetriamine-penta-acetic acid and labeled with either 111In or 90Y. Nude mice bearing intra-abdominal lumps of a human colorectal carcinoma cell line (SW620) were used as a model for peritoneal carcinomatosis. A human monoclonal **antibody IgM**.lambda. (CR4E8) reactive with human squamous-cell carcinoma was used as a control. Indium-111-IgM and 90Y-IgM immunoconjugates were compared in nude mice at 2, 24, 72, 120 and 144 h after i.p. **administration**. Both showed high specific tumor uptake. The tumor-effective half-lives of the immunoconjugates were 39 h for indium and 46 h for yttrium. Tumor-to-normal organ ratios were high and similar for both reagents. Only the **femur** uptake at later time points was relatively higher for the 90Y-IgM than for 111In-IgM. The tumor uptake of specific AC6C3-2B12 was about fourfold higher than the uptake of aspecific CR4E8 at 24 and 120 h. The combination of 111In- and 90Y-labeled AC6C3-2B12 offers a new opportunity to develop safer and more effective methods for diagnosing and treating human patients with peritoneal carcinomatosis.

L23 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:578599 CAPLUS
DOCUMENT NUMBER: 125:241910
TITLE: 99mTc-CD19 monoclonal **antibody** is not useful for imaging of **B cell** non-Hodgkin's lymphoma
AUTHOR(S): Vervoordeldonk, Susan F.; Heikens, Janneke; Goedemans, Wim Th.; Merle, Pauline A.; Von Dem Borne, Albert E. G. Kr.; Van Royen, Eric A.; Slaper-Cortenbach, Ineke C. M.; Van Oers, Rien H. J.
CORPORATE SOURCE: Laboratory Experimental and Clinical Immunology, University Amsterdam, Amsterdam, Neth.
SOURCE: Cancer Immunol. Immunother. (1996), 42(5),

291-296
CODEN: CIIMDN; ISSN: 0340-7004
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In this study we investigated the applicability of 99mTc-labeled CD19 monoclonal **antibody** (mAb) for tumor imaging in patients with **B cell** non-Hodgkin's lymphoma. A 1-mg sample of murine CD19 mAb was labeled with approx. 550 MBq [99mTc]pertechnetate. The labeled mAb was **administered** i. v. to seven patients, four without and three with pretreatment with 10 mg unlabeled CD19 mAb. The no. of circulating B cells was decreased by 44.+-.5% 1 h after injection of the radiolabeled mAb. Peripheral B cells were coated with CD19, resulting in partial modulation of CD19, most pronounced in the three pretreated patients. Whole-body images were obtained with a gamma camera and compared with results obtained by conventional imaging techniques. Initially, blood-pool activity dominated, whereas 24 h after injection the radioactivity was mainly located in the spleen, kidneys and liver. In two patients, a lesion in the spleen appeared as an unlabeled spot. In one patient, a lesion in the **femur** , which was detected by computed tomog. (CT) and gallium-67 scans, was also seen on the CD19 scan from 1 h after **administration** of the radioimmunoconjugate onwards. Good imaging of bone marrow infiltration was obsd. in one of three patients. Lymph node involvement was not obsd. in any of the patients in whom affected lymph nodes were detected by CT or gallium-67 scan. In conclusion, in the present study radioimmunodetection with 99mTc-labeled CD19 mAb was found to be inferior to CT and gallium-67 scanning in the diagnosis of patients with B cell non-Hodgkin's lymphoma.

L23 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:989015 CAPLUS
DOCUMENT NUMBER: 124:84343

TITLE: The bone marrow as a site of antibody production after a mucosal immunization

AUTHOR(S): Benedetti, Ruben; Massouh, Ernesto; Flo, Juan
CORPORATE SOURCE: Laboratory of Immunochemistry, Department of Biological Chemistry, Faculty of Exact and Natural Sciences, University of Buenos Aires, Pabellon II, 4 piso, Buenos Aires, 1428, Argent.

SOURCE: Immunol. Lett. (1995), 48(2), 109-15
CODEN: IMLED6; ISSN: 0165-2478
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To study the importance of the bone marrow in the prodn. of specific **antibodies** after a mucosal immunization with cholera toxin, the **IgG**, **IgA** and **IgM** specific **antibody** forming cells were evaluated by ELISPOT in Peyer patches, mesenteric lymph node (MLN), spleen, blood and bone marrow (BM). When 50-day-old rats were immunized intra-Peyer patches, a similar no. of **IgG** and **IgA** antitoxin **antibody** forming cells (AFC) were found in the BM, whereas in the other lymphoid tissues a higher no. of **IgG** antitoxin was found. In all sites the peak of AFC was obtained 2 wk after immunization. The **administration** of CT to 35-wk-old rats resulted in a stronger immune response in all lymphoid tissues studied, but the proportion of antitoxin AFC contributed by the BM had not changed. One oral dose of cholera toxin resulted in a low

no. of antitoxin AFC, whereas when two or three doses of CT were **administered** orally an increase in the no. of AFC was obsd. in the BM, reaching similar or higher nos. of IgG and IgA AFC than in the spleen. In all cases the highest no. of AFC/106 cells was obsd. in the MLN, whereas antitoxin AFC were not found in the blood. The total no. of AFC recovered from each organ was calcd. taken into account that the BM of one **femur** represents 9% of the total BM. So, it was found that the BM is an important site in the prodn. of **IgG** antitoxin **antibodies**, being the main site in the **IgA** antitoxin **antibody** prodn.

=> fil hom
FILE 'HOME' ENTERED AT 09:56:22 ON 26 FEB 2002

```
ds

Set     Items   Description
S1       3687   BUTTOCK?
S2     222815   HIV OR HERPES? OR CANDIDA OR CHLAMYDIA OR PAPILLOM? OR TRE-
              PONEMA OR GONOCC?
S3         91   S1 AND S2
S4     399399   INJECT?
S5          1   S3 AND S4
S6          1   COLI AND S1 AND S4
S7      10977   THIGH
S8        928   S4 AND S7
S9         12   S2 AND S8
S10      2427   GLUTEUS OR GLUTEAL
S11         2   S4 AND S10 AND S2
S12      5316   S1 OR S10
S13       603   S4 AND S12
S14     50601   GENITAL?
S15         8   S13 AND S14
? s std?

     S16    4155  STD?
? s s1 and s16

            3687  S1
            4155  S16
     S17       2  S1 AND S16
```

15/7/3
DIALOG(R)File 155:MEDLINE(R)

09945177 99023361 PMID: 9808175
Homing of mononuclear cells from iliac lymph nodes to the genital and rectal mucosa in non-human primates.
Mitchell EA; Bergmeier LA; Doyle C; Brookes R; Hussain LA; Wang Y; Lehner T
Department of Immunology, United Medical & Dental Schools of Guy's & St. Thomas' Hospitals, London, GB.
European journal of immunology (GERMANY) Oct 1998, 28 (10) p3066-74, ISSN 0014-2980 Journal Code: EN5
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The route of immunization may affect the type of immunity that is induced. The objectives of this investigation were to establish in the non-human primate if the internal iliac lymph nodes (LN) function as an inductive site of immunity from which mononuclear cells home to the rectal and cervico-vaginal mucosa. Rhesus macaques were immunized with simian immunodeficiency virus (SIV) core antigen p27 in the proximity of the iliac lymph nodes, and compared with the intramuscular (i.m.) (deltoid or gluteal), and axillary LN routes of immunization. The macaques were then challenged rectally or vaginally by a particulate SIVp27 antigen which was applied to the mucosal surface. The tracking dye PKH26 was injected near the immunizing LN or i.m. site and a week later the mucosal and lymphoid tissues were examined at autopsy. Preferential homing of PKH26-labeled cells from the internal iliac LN to the rectal and vaginal mucosa was demonstrated by flow cytometry after targeted iliac LN (TILN) but not after intramuscular (deltoid) or axillary LN immunization. Homing of the subsets of cells revealed that labeled CD4, CD8 and B cells, as well as monocytes were found in the rectum, colon, vagina or cervix. The results of this investigation shows that the route of immunization may affect regional mucosal immunity. Furthermore, the internal iliac LN may function as an inductive immunological site from which CD4, CD8 and B cells may home preferentially to the rectal, cervical and vaginal mucosa, as well as to the related regional but not the unrelated distal LN.
Record Date Created: 19981215
?